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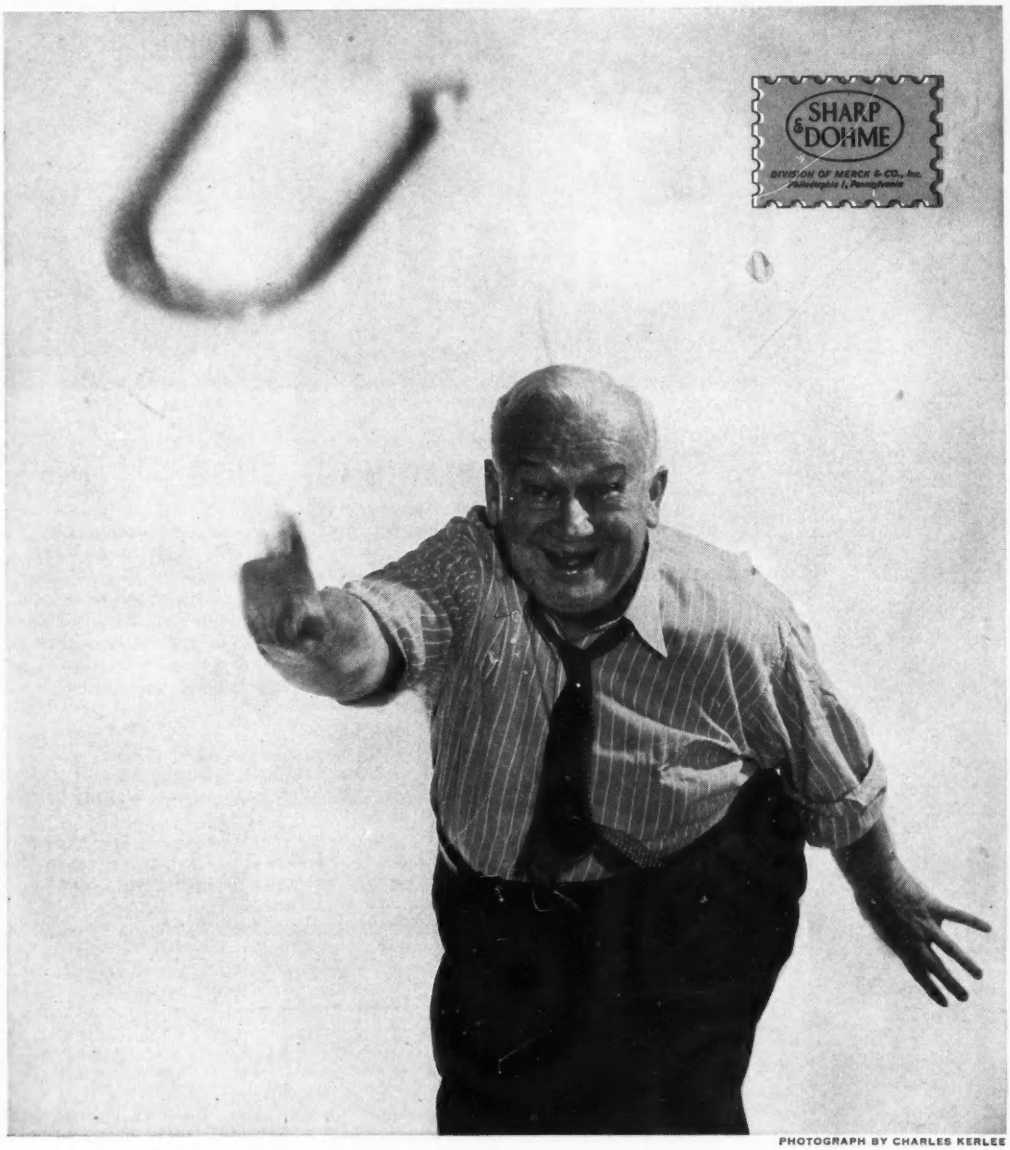

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References: 1. J.A.M.A. 153:185, 1953. **2.** N.N.R. 1953, p. 486.

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Recent Advances in Rheumatic Diseases

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THE MEDICAL PROFESSION has long known that rheumatic diseases pose social and economic problems of major magnitude. Reports from every country where data concerning both incidence and economic loss have been compiled indicate that they are among the commonest causes of protracted illness. From surveys conducted by the Public Health Service, it seems clear that in the United States the rheumatic diseases rank first in incidence and second as causes of disability among the chronic diseases. In this country at least 200,000 persons are totally and permanently disabled, 800,000 more are partially disabled, and a total of about 7,000,000 suffer in some degree from arthritis, rheumatism and related disorders.[75] The burden in terms of medical expenditures, lost wages, and direct financial subsidies is figured to be somewhere around 700 million dollars annually. The Empire Rheumatism Council has estimated that in England and Wales there are about 1,000,000 adult sufferers and that the yearly financial loss is more than 2,000,000 pounds.[21] In Denmark it has been calculated that from 13.5 to 18 per cent of the population has rheumatic disease of one form or another and that 20,000 working years and $25,000,000 are lost to the nation annually as a result.[50] The burden of these diseases in terms of human suffering is, of course, beyond calculation.

Despite their prevalence, however, this group of diseases did not awaken popular interest or incite medical research commensurate with their importance until about five years ago. Interest in the field received great stimulus in 1949 from the discovery of the beneficial influence of cortisone and corticotropin. Lay publicity of this and of subsequent advances, together with the creation of the national Arthritis and Rheumatism Foundation, have done much to arouse public awareness of the problem. Recently unprecedented amounts of clinical and laboratory investigations have been accomplished and the research effort is continuing at an even accelerated pace. An attempt will be made herein to review briefly some of the advances that have been reported during the past year or two as they pertain to the four most common rheumatic diseases.

Submitted October 16, 1954.

RHEUMATOID ARTHRITIS

Many theories have been proposed throughout the years, but the pathogenesis of rheumatoid arthritis remains an enigma. The concept that a fundamental fault resides in the host and that connective tissue elements, particularly interfibrillar substances, react abnormally to injury is currently popular. Stimuli of various types seem capable of inciting the inflammatory reactions of the disease. Infections, emotional stress, trauma, exposure, fatigue, nutritional deficiencies, etc., are frequently related temporally to the onset or to exacerbations, but these are looked upon as activating or aggravating influences, not as actual causes. Recent emphasis has been placed on the relation of psychogenic factors

to precipitation and fluctuations of the arthritis. Despite outwardly normal social and often superior work adjustment, Ludwig[61] found that many victims demonstrate emotional dependence and have pronounced feelings of inadequacy prior to the onset, these phenomena often dating from childhood—and that the onset of arthritis is commonly related to emotional events involving loss of security. Data collected by Stecher and colleagues[88] suggest that heredity may be of more importance than recognized heretofore. They found the disease to be present in 3.1 per cent of relatives of rheumatoid arthritic patients and in only 0.58 per cent of relatives in a control group.

The systemic nature of rheumatoid arthritis is well established. In some severe cases the extra-articular features may be so prominent that difficulty is experienced in distinguishing the process from other connective tissue diseases. Several investigators[5, 76, 97] have found pathologic evidence of diffuse arteritis occurring in patients with rheumatoid arthritis; reportedly, the arterial lesions differ qualitatively from those described for classical periarteritis nodosa in that regional distribution and necrotizing characteristics are lacking.[76] Among others, Ogryzlo[67] observed lupus erythematosus (L.E.) cell reactions in seemingly typical cases of rheumatoid arthritis. The cellular abnormality has been noted also in patients receiving cortisone therapy, the phenomenon sometimes disappearing after withdrawal of the drug.[81] Relation of the phenomenon to steroid administration is far from decided, however, and search for the presence of L.E. cell reactions in a large series of untreated rheumatoid patients might give information as to the specificity of the test and help clarify the issue.

The concept of rheumatoid heart disease has continued to receive support. Evidences of valvulitis and other stigmata are not frequently encountered clinically, but endocardial and myocardial scars indistinguishable from old rheumatic fever lesions, although less extensive, are not uncommon findings at autopsy.[75] Several cases have been reported in which there were active endocardial and myocardial lesions with granulomatous characteristics similar to those found in subcutaneous nodules—and Aschoff bodies were not present.[5]

Reliable statistics regarding the natural history of untreated cases are wanting, but Short and coworkers[79] found that approximately 30 per cent of patients admitted to the Massachusetts General Hospital had had one or more remissions, whereas the disease was essentially progressive in the remaining 70 per cent. Patients whose disease was mild or began with acute or subacute onset were more likely to have lasting remissions—but even after long periods of quiescence relapse was likely to occur. Cited among less favorable prognostic features were insidious onset with gradual progression, persistently active articular manifestations for more than a year, and the presence of subcutaneous nodules.

Data presented by Cobb, Anderson and Bauer[19] discredited the legend that "the way to a long life is to acquire rheumatism." Rheumatoid arthritis is seldom listed as a cause of death, but the mortality rate for persons with the disease was found higher than for the general population; the rate was 24.4 per 1,000 as compared to 18.9 for persons of comparable age and sex. The higher mortality rate was particularly evident in younger age groups and males fared more poorly than females. Valvular heart disease, infections of all sorts, renal disease and pulmonary embolism were notable for their frequency as causes of death among rheumatoid patients; accidental deaths, hypertensive heart disease and myocardial infarction were notably infrequent.

Although not yet practical for routine use, the hemagglutination test may become an important differential diagnostic aid. The procedure is accomplished by titrating the patient's serum with sheep red cells and also with cells to which a "sensitizing" dose of rabbit anti-sheep red cell serum is added. Positive reactions have been noted in about 75 per cent of rheumatoid arthritis patients and false positive reactions are rare.[1, 49] Apparently the agglutinins persist for long periods, even after spontaneous or therapeutic remissions.[18]

TREATMENT

It is recognized that the therapeutic approach to rheumatoid arthritis must be guided by several considerations. As the process is systemic and not confined to joints, local therapy is not enough and measures must be directed against the disease as a whole. While there is no cure, the active manifestations are reversible and with proper management they are amenable to varying degrees of control. No one remedy is effective in all cases and available measures must be selected carefully on the basis of the activity, extent and response of the disease. Often they must be used in combination. The course and responsiveness of rheumatoid arthritis tend to change from time to time and the therapeutic program must be altered accordingly—a regimen appropriate at one phase may not be suitable later.

During the past five years the imagination of scientists has been so stimulated that enormous energy has been expended in quest for a single therapeutic agent—one that has all the advantages and none of the disadvantages of cortisone, hydrocortisone or corticotropin. Similarly, some physicians

have tended to rely on a "one package" remedy and have forgotten to apply the fundamental principles which should govern treatment. Duthie[26] cautioned that, regardless of new adjuncts which may be prescribed simultaneously, such time-tested conservative measures as local and general rest, prevention and correction of deformities by splints, restoration of function by physiotherapy and graduated exercises, avoidance of emotional stress, and sensible well-balanced diet should not be neglected; worthwhile improvement may result from these alone in a substantial number of patients, especially those with mild or moderate disease. Often, however, these supportive measures alone are not sufficient and a physician is forced to resort to potent drugs, among which adrenal cortical steroids, gold and phenylbutazone are popular today.

Adrenal cortical steroids. Although many divergent ideas have been expressed regarding the utility of adrenal cortical steroids in rheumatoid arthritis, the debate, for practical purposes, appears to have terminated. Current opinion is that hydrocortisone and cortisone are highly useful agents in selected cases, especially those in which there is insufficient response to more conservative methods. The question is no longer "if" but "when" and "how best" they can be used.[39] The most discouraging aspects of steroid therapy consist of its frequent failure to terminate the pathologic process, the frequency and severity of relapse when treatment is discontinued, and the tendency toward relative refractoriness in some cases after prolonged administration.[17] Nevertheless, the hormones have impressive assets, the rate of therapeutic response from them is high, and many cases defy control by any other means.

Cortisone by mouth. Statistical data regarding the value of long-term cortisone therapy have varied considerably. Some investigators have estimated that not over 25 to 35 per cent of patients can be maintained in worthwhile remission for two years,[52, 74] while others have concluded that adequate improvement may be maintained in from one-half to two-thirds of patients.[2, 6, 17, 20, 30, 31] This divergency of results is probably explained by differences in composition of the various series in relation to severity and duration of disease, in therapeutic plans and objectives, in methods of dosage regulation, in opinion as to what constitutes satisfactory control and in judgment as to the acceptability and safety of certain hormonal side effects.

Pooled data on 446 cortisone-treated patients from several clinics were analyzed by a special committee of the American Rheumatism Association:[2, 32, 51, 65, 71] Although the statistics were based on results from varied plans of treatment and included experiences with early "trial and error" methods, the information derived was of considerable interest: Benefits were distinctly greater in less active cases; undesirable side reactions were noted in 47 per cent of patients at one time or another; most such reactions were of minor significance but they were sufficiently severe in 18 per cent to prompt discontinuance of therapy; the overall incidence of hormonal complications varied inversely with the size of the daily dose employed, being almost double in patients receiving more than 50 mg. daily as compared to those taking less than this amount; administration was stopped in approximately one-half of the patients—for reasons of complete or almost complete remission in 13 per cent, partial remission in 19 per cent, inadequate benefit in 30 per cent, "worsening" in 6 per cent, "toxicity" in 21 per cent, and for financial, domestic and other causes in 12 per cent.

Results of a more uniformly regulated long-term (six months to four years) study were reported by Bunim, Ziff and McEwen.[17] They found that approximately 50 per cent of patients maintained major improvement or experienced remission, and that 50 per cent had a less satisfactory response. The duration of arthritis prior to therapy was considered as the most significant factor in determining long-range results, satisfactory control being upheld in more than 75 per cent of those with a disease duration of one year or less. Their observations and those of others[30, 52] emphasized that improvement, as measured by subjective relief and increased functional capacity, was strikingly superior to that reported solely on the basis of objective changes in the joints. Frequently functional capacity was enhanced sufficiently to permit good social and economic rehabilitation without proportionate objective improvement and despite, at times, even obvious progression of the disease. As a result of cortisone therapy, functional disability was lessened as follows: the number of bedridden patients was reduced from 17 to 2, of incapacitated nonself-sufficient patients from 31 to 6, and of unemployables from 45 to 11; those who could accomplish full-time jobs increased from 3 to 32. Of 20 incapacitated patients treated uninterruptedly for from one to two years by Copeman and co-workers,[20] 17 were able, with the help of cortisone, to return to their occupations.

An entirely different approach was taken by a group of British investigators.[11, 12, 40] Two small, but carefully controlled, series of patients with early disease (duration not less than three months or longer than nine months) were treated with cortisone and aspirin respectively. At the end of one year the disease was adjudged to be inactive or only slightly active in about three-fourths of the patients of each

group. Conclusions drawn: there was little to choose between cortisone and aspirin in relieving symptoms or in influencing the natural course of early rheumatoid arthritis. These results are not surprising to rheumatologists familiar with the tendency for early mild cases to improve or to undergo spontaneous remission, a fact that has prompted them to recommend first a fair trial with conservative measures.

The failure of maintenance cortisone therapy to cause disappearance of the basic histologic lesions[96, 98, 104] or often to halt pathologic progression in patients with well-established disease, even though functional improvement may be maintained, was emphasized. Using the development of new sites of joint involvement, new subcutaneous nodules and worsening of roentgenographic changes as criteria, Engleman and co-workers[30] noted disease progression in 23 of 56 patients. Bunim and co-workers observed extension of joint involvement in 20 per cent of cases, osseous destruction in previously intact subchondral bone in 30 per cent of cases, and advancement of already existing roentgenographic changes in 40 per cent of cases. Although the degree of rheumatoid inflammation in synovial membranes, subcutaneous nodules, lymph nodes and vascular endothelium may be diminished greatly by the administration of cortisone or hydrocortisone, the histologic changes do not disappear, even after months of therapy, and apparently little or no modification of the basic pathologic pattern of the lesions is induced.[96, 98, 104]

Pseudorheumatism of hypercortisonism. Slocumb[82] described a syndrome consisting of excessive fatigability with weakness, diffuse aching in muscles and joints and emotional instability which he considered as due to hypercortisonism from prolonged cortisone overdosage. Superficially the musculoskeletal symptoms may simulate those accompanying an exacerbation of rheumatoid arthritis but on qualitative analysis they differ, resembling more closely those of psychogenic rheumatism. Slocumb expressed belief that differentiation of "pseudorheumatism" of hypercortisonism from true rheumatoid flares is important, as the former calls for gradual reduction rather than an increase in dosage.

Adrenal cortical suppression. Normally in the case of increased stress, the body requires, and the adrenal cortices produce, increased amounts of adrenocortical steroid. As treatment with cortisone or hydrocortisone temporarily inhibits this normal mechanism during and for varying periods following their use, the administration of additional quantities of these hormones has been recommended in steroid-treated patients subjected to anesthesia, surgical operation, severe trauma, burns and other stressful situations. Several deaths attributable to inadequate protection under such circumstances have been recorded. According to Salassa, Keating and Sprague,[78] it is difficult to decide which patients previously treated with cortisone will have inadequate adrenal response under stress. Pathologic data indicate that adrenal weights usually returned to normal within 20 days after discontinuance of the drug, but atrophy in some cases has persisted longer. They speculated that patients in whom pronounced signs of hypercortisonism develop may be subject to a delayed return of adrenal function. They advised that prophylactic intramuscular injections of cortisone be given in the event of operation or other major stress to any patient who is receiving cortisone (or hydrocortisone) or who has received it in significant quantities within three to six months.

Hydrocortisone by mouth. There is convincing evidence that hydrocortisone, not cortisone, is the principal glycogenic steroid produced normally by the adrenal gland and that it participates predominantly in physiologic reactions incident to stress. Its potency is greater than that of cortisone in equal amount and it appears to have therapeutic advantages. From comparisons of their relative antirheumatic activities in patients with rheumatoid arthritis, the potency of hydrocortisone is judged to be about one and one-half times that of cortisone—in other words, 50 mg. a day of hydrocortisone provides about the same relief as 75 mg. of cortisone.[6] Smaller doses of hydrocortisone than of cortisone are needed for initial disease suppression and for the maintenance of improvement, and results from uninterrupted administration suggest that certain hormonal complications (especially edema, psychic stimulation and abnormally increased appetite) may be fewer and less pronounced. For these reasons some investigators, finding that patients may be managed more easily, prefer hydrocortisone for routine use.[7]

Hoping that information regarding physiologic disposition might afford a better understanding of the relative merits of hydrocortisone and cortisone, Peterson and collaborators[68] determined the rates of disappearance of the two agents from the plasma of normal subjects and of patients with disease. In normal and in rheumatoid arthritic subjects, intravenously injected cortisone disappeared from the plasma twice as fast as hydrocortisone—the difference being ascribed to a more rapid metabolic transformation of cortisone rather than to an increased rate of excretion. Of particular interest was the rate of disappearance in patients with liver disease: cortisone disappeared at its usual rate but hydrocortisone remained in the circulation up to seven times longer. Peterson and co-workers speculated that the long-known ameliorating effects of liver disease with

jaundice on rheumatoid arthritis might be related to decreased metabolic transformation or inactivation of the hydrocortisone which is normally elaborated by the adrenal cortex.

Fluorohydrocortisone. Interest was focused recently on a synthetic halogenated derivative of hydrocortisone—9-alpha fluorohydrocortisone acetate—which possesses powerful anti-inflammatory and salt-retaining activity. Preliminary trials in patients with rheumatoid arthritis have shown that its milligram antirheumatic potency is a number of times greater (roughly ten) than that of hydrocortisone (free alcohol) and that good rheumatic control may be supported with as little as 3 to 7 mg. of the compound a day.[8] Even with these small total daily amounts, however, signs of fluid retention have developed in most of the patients, and they have been pronounced in some. Definite elevations in blood pressure have been noted in about one-half of the patients. The observations indicate that the substitution of a fluorine atom at the ninth carbon position increases the salt retaining property of hydrocortisone to an extent proportionately greater than it enhances its antiphlogistic action. The excessive electrolyte activity of the fluoro compound would seem to preclude its application as systemic therapy for rheumatoid arthritis. The experiences with 9-alpha fluorohydrocortisone acetate are of interest, however, because they demonstrate that the anti-inflammatory potency of hydrocortisone may be enhanced, and other of its properties altered, by a relatively minor modification in its formula. This raises hope that, through other changes in structure or chemical substitutions, a more successful therapeutic agent for rheumatoid arthritis may be produced in the future.

That this hope might be realized sooner than anticipated was suggested recently when Bunim, Pechet and Bollett[x1] reported their experiences with two new synthetic crystalline steroids, metacortandralone (an analog of hydrocortisone) and metacortandracin (an analog of cortisone). Like hydrocortisone and cortisone, the new steroids exert a suppressive, not a curative, influence on the disease, and relapse follows their withdrawal. Preliminary clinical observations, however, indicate that they possess a higher therapeutic index than their parent substances—that is, fewer side effects in relation to a therapeutic dose.

The findings of Bunim and co-workers with metacortandralone and metacortandracin permit only tentative deductions as they were based on short-term studies in but a few patients. Their experience may be summarized as follows: (1) Both substances were found to be highly efficient anti-inflammatory agents. With oral administration subjective improvement was noted within a few hours, and with adequate doses objective response reached a peak within 10 to 14 days. (2) The antirheumatic activity of either compound was estimated to be about three to four times greater than cortisone and two to three times greater than hydrocortisone. (3) Apparently the higher potency was not accompanied by increased hormonal side effects—in fact, the reverse may be true. Total daily doses in the neighborhood of 5 to 25 mg. were sufficient to provide satisfactory rheumatic control and, with short-term administration at least, undesirable effects were negligible. In some of their patients minor endocrine complications, such as faint facial mooning, mild hypertrichosis, and slight acneiform eruption, were noted. Whether these and other unwanted reactions will appear more frequently or more prominently with prolonged therapy remains to be determined. (4) Metabolic balance studies in two subjects failed to demonstrate that metacortandralone influenced either electrolyte or carbohydrate metabolism with dosages of 30 mg. a day or less—but in one subject dosages greater than 30 mg. a day caused a negative nitrogen balance.

Boland and Headley[x2] observed, for short periods, the clinical effects of metacortandracin in 38 patients with rheumatoid arthritis. In general, the early observations confirmed those reported by Bunim and colleagues. Substantially smaller suppressive doses of the new steroid were needed for initial inhibition of the disease. Dosage comparison studies indicated that the potency of metacortandracin is approximately 4.3 times that of hydrocortisone (free alcohol) in equal doses. A number of patients with disease inadequately controlled by hydrocortisone had satisfactory improvement following transfer to the new steroid in smaller milligram doses; and in some instances certain readily reversible side effects, present before transfer, lessened or disappeared. Obviously, however, judgment regarding the true therapeutic efficacy of metacortandracin must await evaluations based on long-term administration.

Trials have been made also with aldosterone (electrocortin), the new mineralocorticoid isolated from the adrenal cortex. Dosages as great as 1,000 micrograms a day given to patients with rheumatoid arthritis failed to promote an antirheumatic response.[x3]

Intra-articular use of hydrocortisone. Instillation of hydrocortisone acetate directly into involved joints has become an important adjuvant in the management of selected cases of rheumatoid arthritis, especially in alleviating inflammatory reactions in one or a few peripheral articulations which may be resistant to otherwise successful systemic

therapy. Local relief results in a high proportion of cases (70 to 89 per cent),[16, 43, 45, 74] but it is usually transient (one to three weeks, occasionally longer). Several less soluble esters have been tried in hope that they would have longer action. Recently Hollander and co-workers[46] reported that hydrocortisone tertiary butyl-acetate sometimes produces a more durable response; in 60 per cent of patients to whom they gave the agent, benefits lasted two to ten times longer than benefits from hydrocortisone acetate.

Information regarding the absorption and local metabolism of hydrocortisone acetate and cortisone acetate has been provided by steroid assays of synovial fluid and membrane made at intervals following intra-articular injections. Both hormones disappear quickly from the synovial fluid, within two to three hours.[33, 100] A large proportion of hydrocortisone acetate is absorbed by the cells of the synovial membrane where it remains for some days. Cortisone acetate is taken up less readily and disappears from the synovial lining much sooner. This difference may partly explain why hydrocortisone is more effective locally than cortisone.[44]

Chromatographic analyses of synovial fluid revealed that hydrocortisone and cortisone, following intra-articular injection, are transformed locally into a number of metabolites.[99] The two steroids present different patterns and apparently much of the injected cortisone is changed to hydrocortisone. These findings prompt a conjecture: Possibly the unique anti-inflammatory effect of hydrocortisone may reside in one of its metabolic products.

Phenylbutazone. Although this drug is now widely employed for the symptomatic relief of various musculoskeletal disorders, its place as a therapeutic agent still awaits final evaluation. Phenylbutazone has strong analgesic and antipyritic properties and exerts some anti-inflammatory action, but a high degree of toxicity has prevented its general acceptance for chronic diseases requiring prolonged administration, such as rheumatoid arthritis.[86] Adverse reactions, some serious and a few fatal, have been observed in from 21 to 40 per cent of cases.* Toxicity is lower when smaller daily amounts are prescribed and there is a growing tendency to limit the total daily dose to 200 to 400 mg.[90]

The results of long-term administration in patients with peripheral rheumatoid arthritis indicate that the drug is less beneficial than originally reported and that its effectiveness frequently wanes with continued use. Symptomatic relief occurs regularly and is better maintained in rheumatoid spondylitis than in the peripheral form of the disease.[56, 84] Holbrook[42] compared results after six months' continuous administration and concluded that the long-range treatment of spondylitis with phenylbutazone was more successful than with cortisone or ACTH. Toone and Irby noted major improvement in 54 per cent of the spondylitic patients but considered that the drug should be employed as an adjunct to, not as a replacement for, x-ray therapy.[62, 95]

Phenylbutazone is rapidly absorbed from the gastrointestinal tract, its peak level in plasma being reached ordinarily within two hours following ingestion; on constant dosage the concentration increases progessively until a plateau is reached on the third or fourth day.[15] When it is given intramuscularly the maximum plasma concentration is not attained for six to ten hours; hence more rapid response should be expected from oral administration. Pharmacologic studies have demonstrated that phenylbutazone probably does not mediate its effects through the adrenal cortex; it does not cause potassium diuresis, eosinopenia, increased ketosteroid excretion or ascorbic acid depletion in the adrenal gland.[15]

Rehabilitation. Lowman and colleagues[59, 60] undertook to rehabilitate severely crippled rheumatoid arthritic patients with active disease. Cortisone or hydrocortisone was administered in maintenance amounts and an intense and comprehensive rehabilitation program was instituted simultaneously. The latter included corrections of joint deformities, muscle building exercises and other physiotherapeutic measures, training in the use of braces and specially devised equipment, vocational instruction and classes in psychosocial readjustment. Of 33 patients trained over a two-year period, 11 were rehabilitated to a completely independent socioeconomic status, two other patients reached a partially independent status, and most of the remaining patients attained noteworthy increases in self-sufficiency.

RHEUMATIC FEVER

Since epidemiologic studies established the fundamental part played by streptococcal infections, it has become evident that the social incidence of rheumatic fever is dependent on the occurrence rate of these infections.[70] The greater risk of streptococcal infections seems to explain the increased frequency of the disease in large families compared with small, and in children attaining school age. Holmes and Rubbo[47] also observed a social pattern in tonsillectomy: The procedure was done more often among children from higher income groups and the incidence of throat infections was distinctly lower among children who had had the operation. Their studies imply that tonsillectomy protects

*References 4, 28, 29, 56, 62, 69, 89, 90.

against rheumatic fever by reducing streptococcal carrier and infection rates.

Studies concerning the natural history of hemolytic streptococcal disease in childhood were reported recently by Rantz.[72] Infections and reinfections with the organism in children under the age of four years were found to be common but associated with relatively mild symptoms and feeble antibody production. In children older than four years the clinical pattern changed so that progressively more of the infections were manifest by acute febrile onset, sore throat, exudative tonsillitis, etc.—together with an increasingly vigorous antibody response. Rheumatic fever was observed in children over the age of four years and not in younger ones—a fact that seems to support the hypothesis that the clinical reaction to hemolytic streptococci is dependent on the type of altered tissue response which is stimulated—this being conditioned by the degree of immunity or hypersensitivity acquired from repeated infections.

The concept that acute rheumatic fever may be prevented by eradicating streptococcal infections, especially of the respiratory tract, together with the advent of efficient antibiotic agents, has allowed major steps to be taken in prophylaxis. Prompt treatment of these infections is now held as the important means of preventing initial attacks. The efficacy of the procedure was demonstrated clearly by Denny and co-workers:[23] Of 798 patients with streptococcal infections treated with penicillin soon after the onset, only two developed acute rheumatic fever; but among 804 patients similarly affected but not treated, the disease occurred in 17. These and other studies have led to the recommendation by the American Council on Rheumatic Fever that persons with streptococcal infections be treated early with penicillin, preferably with a relatively long-acting preparation such as procaine penicillin G in oil.

For the prevention of recurrent episodes, the daily ingestion of small prophylactic amounts of penicillin or one of the sulfonamide drugs has proved dependable. Rationale for this scheme is based on knowledge that approximately 40 per cent of streptococcal respiratory infections are either asymptomatic or so mild that medical care is not sought, and that established infections are frequently neglected.[22] Either of two regimens has been recommended:[38] (a) daily oral administration of a sulfonamide in doses of 0.5 to 1 gram a day, or (b) daily oral administration of 400,000 to 500,000 units of buffered penicillin G, divided into two doses and given on an empty stomach. Kohn, Milzer and MacLean[55] presented evidence which suggested that intermittent administration of penicillin orally may adequately protect the rheumatic subject but more information must accumulate before continuous daily oral administration is discarded.[48] Giving penicillin parenterally has also proved practical in prophylaxis. Using a long-acting repository penicillin, Dipenicillin G ("Bicillin"), Stollerman and Rusoff[92] demonstrated that effective blood levels against Group A streptococci can be maintained for as long as four weeks following a single injection of 1,200,000 units. An injection once each month for two years completely protected from recurrences a group of over 400 patients who had recently recovered from acute rheumatic fever. The method circumvents a major objection to oral therapy—that of relying on the patient for prophylactic medication.[24] The importance of this consideration was emphasized by Dodge and Lichty,[25] who found that in Colorado only 14.5 per cent of children with definite rheumatic heart disease were actually receiving drug prophylaxis.

When streptococcal sore throat develops in a rheumatic subject, treatment with penicillin should be started promptly and continued for a minimum of ten days.[38] Brock and Siegel[13] presented data demonstrating that antibody formation is reduced even though treatment is delayed up to five days. Thus even if therapy of streptococcal sore throat is not begun until relatively late, treatment with penicillin is still indicated.

Treatment of the acute phase. That cortisone, hydrocortisone and corticotropin exert powerful and dramatic suppression of the inflammatory manifestations of acute rheumatic fever has been documented repeatedly. But true assessment of the therapeutic value of these hormones cannot be based on immediate effects alone—it must be measured also by a capacity to shorten an attack, to actually lessen active carditis, and to prevent or reduce residual damage to the heart. As acute rheumatic carditis is a self-limited process and the development of sequelae seems to depend on the duration and severity of the inflammatory bout, prompt inhibition of the acute phase theoretically should lessen myocardial and valvular complications. However, there is still sharp division of opinion as to whether the hormones accomplish this feat—and some authorities even question that hormonal treatment possesses advantages over conventional salicylate therapy.[77]

A preliminary report by the Council on Rheumatic Fever of the American Heart Association, in cooperation with the British Medical Research Council, based on an analysis of approximately 300 cases, stated that a firm conclusion could not be made as to the superiority, any over the others, of salicylates, cortisone and corticotropin in acute rheumatic fever.[66] Although the studies were not sufficiently extensive or over a long enough period to

warrant categorical statement, inference was drawn that each of the drugs promoted about the same degree of immediate improvement and that their influences on the development of residual heart disease were not significantly different. A study by Rowe, McKelvey and Keith brought similar conclusions;[77] they contended that salicylates were just as efficacious and were preferable for routine treatment.

Several outstanding authorities have voiced staunch opposition to such conclusions. Among others, Wilson and co-workers[101, 102] believe that the hormones favorably alter the natural course of the disease and when given early, in sufficient amounts and for long enough periods, they will arrest active carditis and prevent or lessen the development of chronic cardiac sequelae. They presented a strong case: Of over 1,500 patients with authentic rheumatic fever and rheumatic carditis treated with salicylates, not one following recovery from the acute phase had a normal heart according to the strict criteria of the American Heart Association. In the experience of these investigators it has been only since the advent of the hormones that they have observed cases in which there was full recovery, without evidence of residual heart disease.

Interesting studies on the concentrations of circulating adrenal cortical hormones and of corticotropin in patients with rheumatic fever were reported by Kelley.[53] During the first week of the disease, the amount of 17-hydroxy corticosteroids in the blood is elevated as compared to normal controls, but after two weeks, when the disease becomes well established, it is reduced considerably below normal. Concentrations of endogenous circulating corticotropin are elevated throughout the course. These findings were interpreted to mean that patients with rheumatic fever have relative adrenal insufficiency—a situation comparable to that which exists in patients with Addison's disease and following adrenalectomy in that steroid concentrations are low and corticotropin concentrations are high. These observations led Kelley to suggest that adrenocorticosteroid administration might be considered as replacement therapy. The residual cardiac status of patients treated with hormones was compared with that of patients treated by conventional methods, including salicylate administration. During the acute phase 100 per cent of the hormone-treated group and 96 per cent of the nonhormone group had murmurs. When discharged from the hospital, the incidence of murmurs for the two groups was similar—71 per cent for the nonhormone and 66 per cent for the hormone-treated series. Thereafter the incidence in the nonhormone-treated group changed but little whereas it decreased progressively in the hormone-treated group until at the end of a year only 9 per cent had residual murmurs.

"C-reactive protein," so-called because of its capacity to form a precipitate with the C-polysaccharide of pneumococci, appears in human serum as a nonspecific inflammatory response. Stollerman and colleagues[91] expressed belief that the test provides a sensitive and reliable gauge for rheumatic activity if other inflammatory processes can be excluded. The disappearance of this protein from the blood marks the termination of a rheumatic attack but does not preclude recurrences.

OSTEOARTHRITIS

There have been few significant recent advances in knowledge of osteoarthritis or in the treatment of it. Histological and chemical investigations have provided some information regarding the fundamental changes which occur in the cartilage. Electron microscopic studies have demonstrated that with aging there is a gradual and irregular loss of the amorphous mucoid material responsible for the binding of water in cartilage. Matthews observed that cartilage degeneration is associated with disappearance of a mucopolysaccharide, chondroitin sulfate;[64] and, since much of the elastic property of the tissue seems to depend on the presence of this substance, loss of it may account for the decreased resilience and increased susceptibility to wear and tear which accompanies the aging process.[27]

Sir Russell Brain in his Heberden's Oration of last year gave a brilliant exposition of the possible mechanisms involved in the development of radiculitis secondary to osteoarthritis of the cervical spine.[9, 10] Although recognizing the possible effect of posterior spurs as they may encroach on the posterior intervertebral foramina, he pointed out that the nerve roots normally occupy only one fifth to one-fourth of the diameter of their foramina and hence considerable narrowing of the apertures can occur without causing compression. He emphasized that radicular nerves within the foramina may be displaced as a result of cervical disc degeneration, quite independently from any pressure from disc protrusion. With narrowing of the cartilaginous discs, the spinal cord and dural sac retain their original length while the spine itself is shortened—this may result in a sharp angulation of the nerve roots and, with the associated ischemia, may lead to irritation or degeneration of nerve fibers. At times the sheath of the nerve undergoes fibrosis in the region of involvement, causing adhesions between the nerve root and its covering. This condition has been termed "root sleeve fibrosis" and, in Sir Russell's opinion, it is frequently responsible for the brachial

neuritis or neuralgia which is observed in association with cervical osteoarthritis.

Li and co-workers reported very interesting studies on the production of osteoarthropy in adult female rats with the administration of large doses of anterior pituitary growth hormone.[3, 73] After receiving the hormone for approximately a year, the animals had abnormalities in the joints of the knees, ankles and spine, principally irregular articular surfaces, thickened joint linings and multiple exostoses. In certain respects the abnormalities bore resemblance to osteoarthritic changes as seen in man.

GOUT AND GOUTY ARTHRITIS

Modern methods of genetic analysis have helped to explain the seemingly inconsistent inheritance pattern of gout. The frequency of asymptomatic hyperuricemia among members of families with patients with overt gout has been shown to be high (25 per cent or more). Stecher and co-workers found that the inherited, dormant hyperuricemia has a penetrance of about 84 per cent in men and 12 per cent in women.[87] Moreover, a sex difference seems to exist with respect to purine metabolism, for serum urate levels in both healthy and gouty subjects are significantly lower in females than in males. According to Gutman,[35] this may be related to a higher urate clearance rate in females and possibly to a variation in urate biosynthesis. Not answered, however, is the question as to why some males with hereditary hyperuricemia develop clinical evidences of the disease while others do not.

Information has been obtained also regarding the nature of the anomalous purine metabolism in gout. The problem has been approached by employing isotope tracer techniques, determining the fate of tagged precursors of uric acid and of labeled uric acid itself.[35, 37, 58] A variety of metabolic precursors for uric acid have been identified, many of them being relatively simple and readily available substances. Such studies have indicated that the bulk of urate production, normally and in gout, results from the endogenous biosynthesis of simple nonpurine precursors—a fact which precludes the possibility of controlling urate overproduction by dietary regulation alone. Nevertheless, the dietary intake of preformed nucleic acids and purines is still considered to have an important accessory influence on the course of the disease since the heavy ingestion of these substances increases urate production greatly (by as much as 100 per cent in some instances), the extra burden leading to further rise of serum urate levels and to accelerated accumulation of urates in the tissues.

Whereas it is understood that the clinical and pathologic manifestations of chronic tophaceous gout are related to supersaturation of urates in interstitial fluids and the deposition of them in such structures as joints, bursae, cartilage and renal parenchyma, the pathogenesis of acute bouts of gouty arthritis remains obscure. Several clues have prompted speculation that a temporary adrenal cortical deficiency may be implicated in the development of acute seizures.[41] Common precipitating factors are trauma, surgical operation, infection, allergic reaction, psychic upsets and exposure to cold or heat—each of which produces stress with its associated sudden increase of adrenal cortical secretion, followed by a decrease to subnormal levels. Furthermore, acute attacks may be suppressed by the administration of corticotropin, and the urinary excretion of 17-ketosteroid is subnormal in gouty patients. From these observations inference has been drawn that a relative deficiency of adrenal cortical secretion or a diminished target responsiveness to the hormone may exist at the time of an acute bout.

By the use of one of three medicinal agents—colchicine, phenylbutazone and corticotropin — it is possible to control effectively, or terminate quickly, most acute seizures of gouty arthritis. Less than 5 per cent of acute attacks fail to respond to a single full therapeutic course of colchicine, but results are not always complete, especially if treatment is delayed.[35] Intravenous colchicine has proved to be a safe, rapid and efficient antidote in the acute phase, and according to Graham and Roberts[34] deserves wider application—especially when prompt response is required and when severe gastrointestinal intolerance prohibits oral administration. With the usual single intravenous dose of 3 mg., unpleasant side effects are rarely observed.

The efficiency of phenylbutazone in acute gouty arthritis approaches that of colchicine. Currently recommended oral dosage is 0.6 to 0.8 gm. daily for five to ten days, or for shorter periods if recovery occurs sooner. Kuzell and colleagues observed major improvement in 83 per cent of patients, and 41 per cent were free of symptoms within 48 hours.[56, 57] Similar statistical data on results have been published by others.[54, 90] Relief appears to ensue even more rapidly following intramuscular administration of the drug. A single injection of 0.5 to 1.0 gm. given at the beginning of an attack may suffice; in resistant cases or when treatment is delayed, reinjection on two or three successive days may be needed. Most authorities consider phenylbutazone as a second choice to colchicine and, because of its potential toxicity, emphasize caution in its use.[90] They concede, however, that for the brief treatment required in acute gouty arthritis the risk is small.

When given early and in adequate amounts, corticotropin will suppress most acute bouts. As sud-

den termination of the hormone is often followed by an articular relapse, it is necessary, after two or three days of full doses, to taper off the dosage gradually over a period of several days and to administer small amounts of colchicine by mouth simultaneously. Corticotropin probably should be reserved for special cases which are resistant to colchicine and phenylbutazone.[90]

An acutely inflamed gouty joint may respond dramatically when hydrocortisone acetate is injected intra-articularly. The procedure is sometimes useful in the management of stubborn attacks but should be employed as an adjunct to, not as a substitute for, standard therapy.[16, 45, 80]

The management of gout during the intervals between attacks is directed toward (1) preventing or reducing the frequencies of acute episodes, (2) controlling hyperuricemia so as to minimize the deposition of urates in the tissues, and (3) if possible, mobilizing deposits which are already formed. No set regimen is applicable to all patients with gout—rather, the restrictions imposed and the medicaments prescribed should be tailored to fit the severity and responsiveness of the individual process.

The lively biosynthesis of uric acid from simple precursors present in virtually every foodstuff necessarily limits the value of dietary regulation. Nevertheless, the intake of foods rich in preformed purines and the nitrogenous precursors of uric acid should be restricted.[35] Fat consumption should be limited also because excessive amounts cause renal retention of urates and tend to increase the incidence of acute seizures.[93, 94]

Colchicine given uninterruptedly in low dosage is the most effective agent available for lessening the recurrence rate of acute attacks.[75, 80, 93, 94] With daily prophylactic amounts ranging from 0.5 to 2.0 mg., Gutman observed striking reduction in both the frequency and severity of seizures in over two-thirds of patients.[35]

Because of its analgesic properties, apparent ability to lessen the frequency of acute bouts, and its uricosuric action, some investigators have advocated phenylbutazone as "maintenance" treatment for interval gout. Reports of long-term studies are few, but the opinion of most observers is that, in light of the potential hazards from the drug, continuous and indefinitely prolonged administration is not justified. Furthermore, urate clearance studies made by Yu, Sirota, and Gutman and others indicate that the uricosuric action of phenylbutazone is highly variable and distinctly inferior to that of probenecid.[36, 63, 85, 103]

Laboratory and clinical investigations have been sufficiently extensive to establish probenecid (Benemid®) as the most suitable uricosuric agent available in chronic tophaceous gout.[35, 41, 80, 83, 90, 93, 94] The drug causes a pronounced and selective suppression of tubular resorption of urates, which results in an increased rate of urate excretion by the kidneys. This is accompanied by a lowering of serum urate values which may be maintained by continuous administration of the drug. The toxicity of probenecid is low with the usually recommended dosage of 0.5 to 2.0 gm. a day, but amounts larger than 2 gm. a day may cause nausea and anorexia.[93]

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Gastric Polyposis

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• In a series of 48 cases of gastric polyps, 40 patients had benign lesions while the polyps in the remaining eight cases were malignant. Although the symptomatology in this series was not uniform, only one patient was entirely asymptomatic. Of the eight patients with malignant lesions, three had polyps which could well be described as small, suggesting that size may not be a reliable criterion of benignity even in a single lesion.

Laboratory studies indicated that anemia, achlorhydria and occult blood in the stools are frequently associated with gastric polyps. There was no apparent correlation, however, between these phenomena and the benign or malignant nature of the lesions.

X-ray examination, performed in every instance, was completely negative in six cases and inconclusive in an additional five. Gastroscopy did not reveal the presence of polyps in three of 15 cases. Malignant change was detected by cytologic examination in one case in which both roentgen and gastroscopic examination were negative.

The author believes that in most cases of gastric polyps operative treatment affords the greatest degree of safety. An operative procedure of considerably less extent than total gastric resection often is feasible. However, if true polyps occur where removal can be effected only by total gastric resection, the incidence of malignant change in these lesions would seem to indicate the advisability of such a procedure unless positive contraindicating conditions are present.

ALTHOUGH GASTRIC POLYPS were first identified at autopsy in 1761, almost a century elapsed before the first clinical diagnosis was made. Even with the advent of roentgenoscopy, first used in the diagnosis of gastric polyps in 1911 by Heinz,[11] and more recently of gastroscopy following Schindler's successful application of this method in 1922,[1] antemortem diagnosis has remained relatively infrequent. Most investigators agree that the reported incidence does not reflect the true occurrence of these lesions, since they tend to produce only mild symptoms or to remain completely asymptomatic for long periods.

Opinion has been considerably more divergent, however, regarding the preferred method of treatment. Behind this disagreement lies the crucial question of whether benign gastric polyps may act as precursors of carcinoma or undergo malignant degeneration with sufficient frequency to warrant surgical removal.

A review of the literature in 1950 by Edwards and Brown[3] emphasized the long-standing division among investigators on this vital point. Many believe that most benign-appearing gastric polyps should be surgically removed owing to the incidence of malignant degeneration and the uncertainty of all available diagnostic procedures in detecting malignant transformation.[3, 7, 8, 13] Since Brunn and Pearl[1] published their comprehensive report in 1926, various investigators have reported manifestations of malignant change in from 6 per cent to 51 per cent of cases.[9] Edwards and Brown[3] felt that gastric carcinoma frequently occurs in association with benign gastric polyps and that malignant degeneration may take place in apparently benign lesions. In 1951, Klein and Geller[7] described a case which they believed afforded clinical demonstration of malignant transformation. In a discussion of cases observed at Lahey Clinic, Marshall[8] (1952) reported that 30 per cent of the gastric polyps removed by excision or partial gastric resection were malignant.

At the same time, other investigators expressed the opinion that malignant degeneration is sufficiently unlikely in benign polyps to make conservative treatment the procedure of choice in many instances.[2, 6, 9] A recent article by Hay[6] (1953) emphasized this view and the clinical factors upon which it rests. After observing asymptomatic patients with benign-appearing lesions who were subjected to operation on the grounds that the lesions might be precancerous, Hay felt that the risk of surgical treatment might be greater than that of malignant degeneration and undertook a further study of the differential diagnosis between benign and malignant adenomas. He concluded that those patients who are asymptomatic or mildly symptomatic, with polyps less than 2 cm. in diameter which appear benign to the gastroscopist and the roentgenologist should not be operated upon, but should

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TABLE 1.—*Gastric polyps, 1919-1951*

	Single	Multiple
Men	7	18
Women	13	10
Total	20	28

TABLE 2.—*Symptoms of gastric polyps*

	Benign	Malignant
Epigastric distress—fullness, nonradiating pain, heaviness	21	4
Abdominal pain	7	1
Anorexia and nausea	3	5
Vomiting	4	4
Diarrhea	6	1
Tarry stools	2	3
Weakness	3	2
Constipation	3	1
Belching and sour stomach	5	1
Dyspnea	4	..
Weight loss	2	2
Dysphagia	1	..
Asymptomatic	..	..

be observed every three to four months for the first year and biannually thereafter. He favored operation if the polyps are larger than 2 cm. in diameter, if malignancy is suspected on the basis of gastroscopy or x-ray examination, if the clinical symptoms are severe, and in patients who cannot be adequately followed.

Recent observation of a degenerative course in three patients who at original clinical examination appeared to have benign gastric polyps prompted a review of all cases treated on the Medical and Surgical Services of the University of California Hospital during the last three decades.

During the 32-year period from 1919 to 1951, 48 patients with gastric polyps were observed. In 40 cases the polyps were benign, in eight, malignant. As indicated in Table 1, the series as a whole closely reflects the equal incidence in men and women cited by several investigators. However, there was a considerably higher incidence of multiple polyps in men than in women. The largest single group was made up of patients in the seventh decade of life. The youngest patient in the series was 16 years of age, and the oldest was 77, while the average age was 55 years. The distribution by decades was as follows: 10-19 years, one patient; 30-39, seven; 40-49, ten; 50-59, eight; 60-69, fourteen; 70-79, eight.

The symptomatology of gastric polyps is neither clear-cut nor uniform. Table 2 summarizes the symptoms observed in the present series. Epigastric distress, present in over half of the cases in the series, is probably the complaint most frequently encountered upon clinical examination, as has been noted in other reports. Abdominal pain, anorexia and vomiting or nausea each occurred in eight cases, while diarrhea, the next most prevalent symptom, was present in seven cases. Only one patient with gastric polyps was free of symptoms referable to

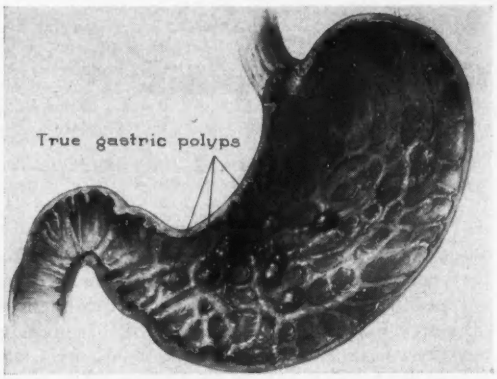

Figure 1.—The adenomatous nature of this type of gastric polyp is evident. The mucosa is either normal or somewhat atrophic.

the stomach. This is in striking contrast to some reports in which approximately 45 per cent of the patients with benign lesions were considered asymptomatic.[6]

It is characteristic of gastric polyps that symptoms may persist for many years. In the present series six patients had had varying degrees of discomfort for more than ten years; four for five to ten years; six for two and a half to five years; ten for one to two and a half; nine for six months to one year; nine for one month to six months, and three for less than one month. There were two patients with malignant lesions in this group, one of whom had had epigastric distress for 20 years, while the other had had sour stomach and flatulence for as long as 11 years. One patient with a benign lesion had had constipation for 30 years and abdominal pain for six; another whose polyp was benign had had epigastric distress for 15 years. A recent increase in severity of symptoms had occurred in seven cases, three of which were subsequently proved to be malignant. From our series, it would seem that neither the duration nor the severity of symptoms in gastric polyps is sufficient to provide a basis for differential diagnosis as to malignant or benign lesions.

Most reports in the literature have indicated that gastric polyps are only rarely associated with polyps elsewhere in the intestinal tract. In this series gastric polyps occurred in association with polyps in other segments of the intestine in only four cases—in the rectum in two cases and in the duodenum in two.

From the standpoint of malignant degeneration, the pathologic features of these lesions are especially significant. In 1888, Menetrier identified and described two kinds of multiple gastric polyps.[1] One type is composed of discrete lesions scattered over the surface of the mucosa. The polyps may arise from the mucosa by pedicles of varying length, or may lack this stalklike structure entirely and emerge broad-based from the mucous membrane (Figure 1).

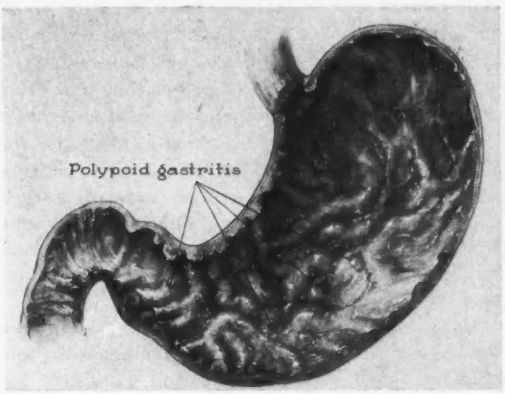

Figure 2.—Note the irregular plaque-like masses superimposed upon the hypertrophied gastric mucosa.

In the second type, the polyps occur as clearly defined plaques or masses on the periphery of the folds of hypertrophic mucosa (Figure 2). The precise nature of these two patterns of overgrowth of gastric mucous membrane, namely, the true adenomas (Figure 3) and the inflammatory hyperplasias, has been a matter of considerable discussion. In the latter instance, the pathologic changes are those of hyperplastic chronic gastritis, wherein hyperemia and edema of the enlarged and tortuous gastric rugae are prominent features (Figure 4). Although polypoid gastritis is not neoplastic in itself, but rather represents areas of metaplasia and irregular clusters of cells, true adenomas developing upon the hypertrophic gastric folds have been described by some investigators. Undoubtedly some cases previously described as gastric polyps have in reality been polypoid hypertrophic gastritis. Although such conditions may seriously affect health, there is general agreement that there is less risk of malignant change in polypoid gastritis than in true adenomatous polyps of the stomach.

It is unfortunate that so ambiguous a term as "gastric polyposis," which has been used to indicate multiple polyps of either type, has been so widely adopted. Had the two terms "polypoid adenomas of the stomach" and "polypoid gastritis" been consistently applied instead, there would undoubtedly have been far less confusion as to the exact type of pathological entity involved.

Some investigators have used the term "polyposis" to apply only when three or more polyps were present and have classified cases of two polyps as single. It is the author's feeling, however, that any case in which there is more than one polyp should be considered as multiple. Cases are so tabulated herein. Thus in this series, there were 28 cases in which more than one polyp was present; in 14 of them the lesions were discrete, while in the remaining 14 diffuse polyposis was present in association

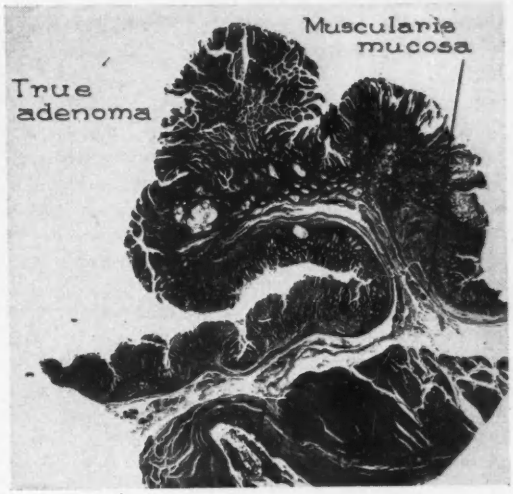

Figure 3.—The villous nature of this type of true polyp is evident. The stalk includes the muscularis mucosae. Edema and increased vascularity are not prominent features.

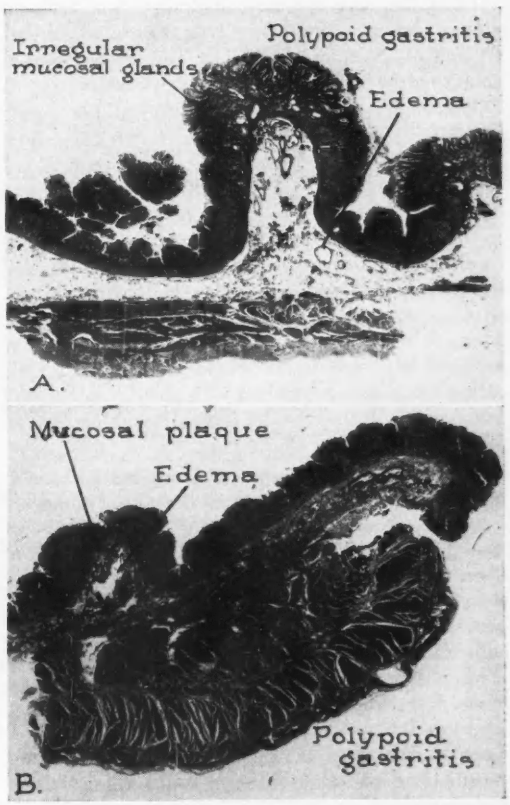

Figure 4. *A*—Note the edema and the enlarged vascular channels in the submucosa extending up as a stalk to form a pseudopolyp. *B*—The mucosal glands are distorted and hypertrophied.

with hypertrophied gastric mucosa. Four of the patients in the former group had two polyps each, while nine had from three to six polyps and one had 15.

Laboratory studies have demonstrated some uniformity of findings in gastric polyps, both in the present series and in reports of other investigators. The results of blood studies in 37 cases were available. In 18 cases the hemoglobin content was within normal limits, while in 19 cases varying degrees of anemia were observed. Of the eight patients with malignant lesions, four had subnormal hemoglobin content (values as low as 74 per cent) while three were within normal limits and in one case the data were not available. However, in this series, some patients with benign disease had greater degrees of anemia than did those with malignant lesions. Of the patients with benign lesions six had hemoglobin values of less than 65 per cent, while in one case the value was as low as 12 per cent.

Achlorhydria was frequently present. No free acid was detected in 27 of 32 cases in which gastric analysis was done; in the other five acidity was normal. The lack of gastric acid appears to be even more common in multiple polyps than in actual carcinoma of the stomach; in fact Tempest[11] reported achlorhydria in about 95 per cent of cases.

Laboratory records of stool studies for occult blood were available in 40 cases. In 24 the results were negative; in 14 the reaction for occult blood ranged from 1 plus to 4 plus, and in two others was "strongly positive." No occult blood was detected in four of the eight patients with malignant polyps; results were positive in two cases, and in the remaining two no data were available. Of the five patients with occult blood of 4 plus, four had benign lesions. Thus, it would seem apparent that while anemia, achlorhydria and occult blood in the stools are rather frequently associated with gastric polyps, the findings are by no means indicative of benign or malignant nature of the lesions.

Much of the discussion concerning malignant degeneration has hinged around the effectiveness of roentgenographic and gastroscopic examination in establishing a differential diagnosis.[2, 8] In the report upon their first series Brunn and Pearl stated that a definite abnormality had been observed in every case in which x-ray studies were accomplished. Their subsequent observations, however, indicated that a definite diagnosis could not always be made by this means.[10] Edwards and Brown[3] reported that x-ray investigation was diagnostic in 55 per cent of 31 cases on first examination, or 84 per cent including "suspicious" cases and those in which filling defects were noted.

In the present series, roentgenographic examination was performed in every instance. In 32 (66 per cent) polyps were indicated in the first examination. In an additional five cases, the polyps were misdiagnosed as another disease or overlooked entirely, while in five other instances polyps were identified only as "growths" or "filling defects." In six cases (12.5 per cent) the roentgenogram was negative for any disease of the stomach. Of the eight patients with malignant lesions, polyps were diagnosed roentgenographically in six, while filling defects were noted in the remaining two. In two instances, the possibility of malignant disease was indicated on the basis of the roentgen examination.

Gastroscopy was performed in 15 cases in this series. In three cases, gastroscopic diagnosis was negative, while x-ray examination indicated the presence of polyps. Similarly, in three other cases the x-ray diagnosis did not indicate any disease of the stomach, whereas polyps were detected by gastroscopy. In one additional case, the abnormality was diagnosed as ulcer on x-ray examination but identified as polyps by gastroscopy. This comparison would serve to support the view expressed by Paul and Logan[9] and others that the two methods are complementary as diagnostic procedures. More significant, however, from the standpoint of this analysis is the fact that in an appreciable proportion of cases, both methods may fail to reveal the presence of the gastric lesion. In one series reported in the literature, the benign or malignant nature of the polyps could not be diagnosed by either technique in approximately one-third of the cases.[5]

Most investigators who favor a period of medical observation for the majority of benign cases usually base their decision as to which lesions should be treated nonsurgically in part on the size of the polyp. In the present series the largest single lesion was approximately 10 cm. in diameter, while in six cases the polyp was 2 cm. or less in diameter. In six other cases no indication of size was recorded, while the remainder of the single lesions were between 3 and 7 cm. Of particular significance, however, is the fact that in three of the cases in which there was evidence of malignant degeneration the polyps were 2 cm. or less in size. In one case, one polyp was present; another involved three polyps, while in a third case of discrete polyposis none of the polyps observed exceeded 2 cm. The experience in this limited number of cases suggests that the size of the lesion has no definitive diagnostic relationship to possible malignant degeneration.

Recently the author applied cytologic examination as a method of studying gastric polyposis. By means of papain lavage, rich cellular material from the gastric mucosa may be obtained for direct observation. This technique has proved its effectiveness in detecting malignant disease when both x-ray and gastroscopic studies have been inconclusive (see

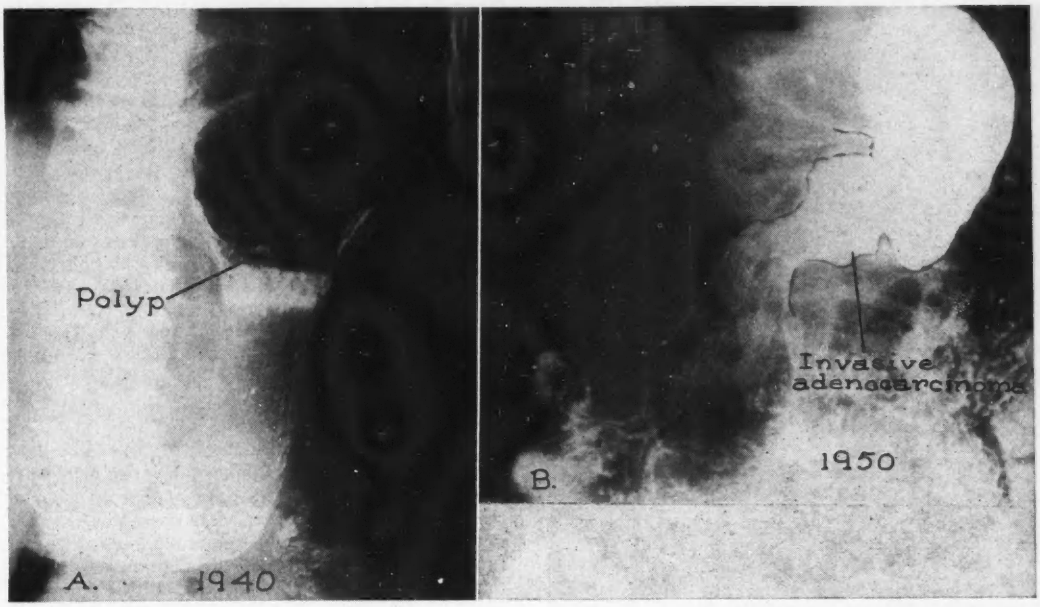

Figure 5. *A*—**Polyp on the anterior wall of the upper stomach.** *B*—**Repeat x-ray studies in the presence of clinical symptoms demonstrated a large infiltrating gastric carcinoma in the exact site of the gastric polyp noted ten years previously.**

Case 2 below). Papain lavage was not used in a sufficient number of cases in the series to warrant definitive conclusions. However, it has proved of value in the diagnosis of gastric cancer.[4] It is to be anticipated that as increasing numbers of cases are observed by this method, it may well provide a means of further establishing benignity or malignancy of gastric polyps and a technique which can be applied to the detection of malignant change in subsequent follow-up of benign cases.

At present, however, the possibility of malignant degeneration seems sufficiently established, and the detection of polyps or the malignancy of polyps sufficiently uncertain as to make surgical removal necessary to insure the greatest degree of safety for most patients. Three cases in the present series particularly emphasize the tendency of benign polyps to undergo malignant change. A detailed review of these cases is presented below:

CASE REPORTS

CASE 1. The patient, 67 years of age, was observed in the out-patient department on June 15, 1940, at which time a small area of tenderness was noted on deep palpation directly over the epigastrium. X-ray examination indicated pronounced hypertrophic gastritis with a questionable small soft tissue mass in the fundic portion of the stomach. The patient refused gastroscopy. On May 13, 1941, a second x-ray examination revealed a polyp 12 mm. in diameter on the anterior wall of the stomach 7 cm. below the diaphragm. This diagnosis was confirmed by two subsequent roentgenograms. Operative removal was suggested but the patient refused.

Ten years later, in June 1951, the patient was observed in the surgical clinic. For the previous six months she had noticed epigastric distress, not particularly related to meals. Progressively increasing dysphagia had been present for three months; during the preceding three weeks the patient had only been able to take fluids and had had frequent regurgitation. There had been a recent loss of weight, but neither hematemesis nor melena was present.

X-ray examination was again carried out, and the diagnosis was obstructing carcinoma of the upper stomach invading the esophagus. At this examination the radiologist observed, "It is very interesting to note that ten years ago this patient was examined in this department and a single small polyp was seen in the exact location of the present carcinoma" (Figure 5). Exploratory laparotomy was carried out but the growth was so extensive that only palliative gastrostomy was done. The pathologist's report confirmed the x-ray diagnosis of carcinoma at the cardioesophageal junction.

This case, which is similar to that reported by Klein and Geller,[7] would seem to provide clinical demonstration of malignant degeneration of a gastric polyp.

CASE 2. A 65-year-old woman entered the hospital on June 18, 1951. Her history indicated that 20 years previously she had noted an episode of epi-

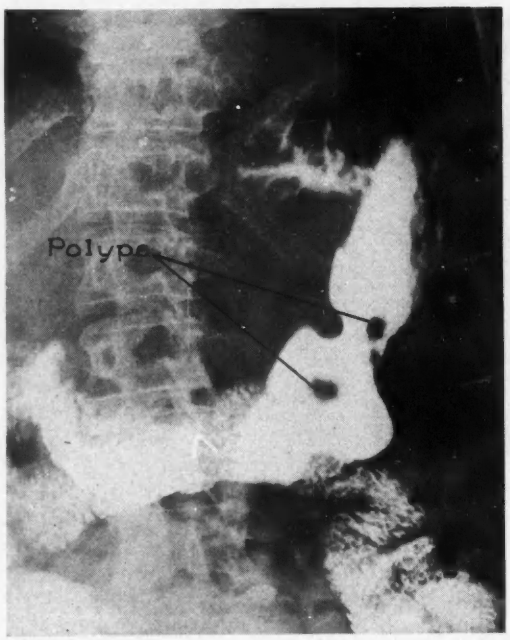

Figure 6.—The two polypoid masses were demonstrated by gastrointestinal study. Preoperative cytologic study indicated the presence of "cells suspicious for malignancy." Numerous true adenomas, one of which was malignant, were found at operation.

gastric heaviness after eating, and loss of appetite. At that time a diagnosis of atrophic gastritis was made, and the patient was treated for vitamin deficiency. In 1947 x-ray and gastroscopic examination had been performed and gastric polyposis was diagnosed. Films taken in 1948 and in May 1951 also showed the polyps. Just before hospitalization, a series of "nervous upsets" had brought on a recurrence of indigestion. The patient had never had vomiting, hematemesis, severe abdominal pain, constipation or melena. Symptoms were confined to the upper abdomen. The patient said that she had a "total lack of acid" and that she took hydrochloric acid with each meal. There had been no significant loss of weight.

X-ray examination on the day following admission again indicated gastric polyposis (Figure 6), and the radiologist noted that two of the polyps in the pars media appeared larger than in previous films. Two days later gastroscopic examination was performed. No evidence of infiltration was observed, but in comparison with the gastroscopic examination of June 1947, the polyps on the angulus appeared to have increased in size, and there were others on the posterior wall that had not been noted on previous examination. The gastroscopic diagnosis was gastric polyposis and general atrophic gastritis. Neither x-ray nor gastroscopic examination indicated possible malignancy.

Cytologic examination was then performed, using the papain lavage technique. Among the material aspirated from the gastric mucosa, several cells "suspicious for malignancy" were detected.

On June 25, 1951, operation was carried out. Numerous polyps, all entirely within the distal three-fifths of the stomach, could be palpated through the intact gastric wall. Because of these findings and the preoperative indication of possible malignant change subtotal gastrectomy was carried out.

Upon examination of the pathologic specimen multiple sessile polypoid structures up to 1.0 cm. in diameter were noted on both the anterior and the posterior gastric walls. There was a polypoid mass 2.0 cm. in diameter on the anterior wall. Microscopically, irregular areas of thickening and thinning of the gastric mucosa were observed. The sessile polypoid masses were composed of redundant mucous glands. Some of the cells showed a variation in total as well as nuclear size. In one polyp there were some papillary proliferation in one dilated gland structure near its surface. Multiple papillary projections and much cellular pleomorphism were present, and mitoses were frequent. No invasion of the submucosa or muscular coats was noted, and the lymph nodes along both greater and lesser curvature contained no metastatic malignant cells.

In the foregoing case of multiple gastric polyps, although only one lesion proved to be malignant, preoperative cytologic examination indicated the possibility of malignancy.

CASE 3. A woman 67 years of age was admitted to the University of California Hospital on March 3, 1951, for abdominal exploration on the basis of x-ray (Figure 7) and clinical findings. She had been seen in the surgical clinic on February 20, at which time she reported a loss of 25 to 30 pounds in body weight during the preceding six months. Considerable nausea and anorexia had occurred, but the patient had had only one episode of vomiting with hematemesis during that time. Occasionally a vague sense of epigastric fullness had been present, and diarrhea usually lasting two to three days had occurred about once a week.

The patient was operated upon March 5. When the peritoneal cavity was entered a small polyp was observed in the prepyloric area, and subtotal gastrectomy was carried out; three-fourths to four-fifths of the stomach was removed. The specimen was examined and found to contain two polyps in the antral area. There was a third small polyp on the posterior gastric wall immediately above the proposed line of anastomosis. It was decided, however, that total gastric resection, which would have been necessary in order adequately to excise the remaining lesion, was not indicated. This small lesion was therefore coagulated by means of the electrosurgical unit and an antecolic Mayo-Polya anastomosis was carried out. Pathological diagnosis indicated two gastric polyps, both of which showed focal adenocarcinoma in situ.

The patient was examined in the surgical clinic every six months after operation without evidence of recurrence until January 1954, when obstructive

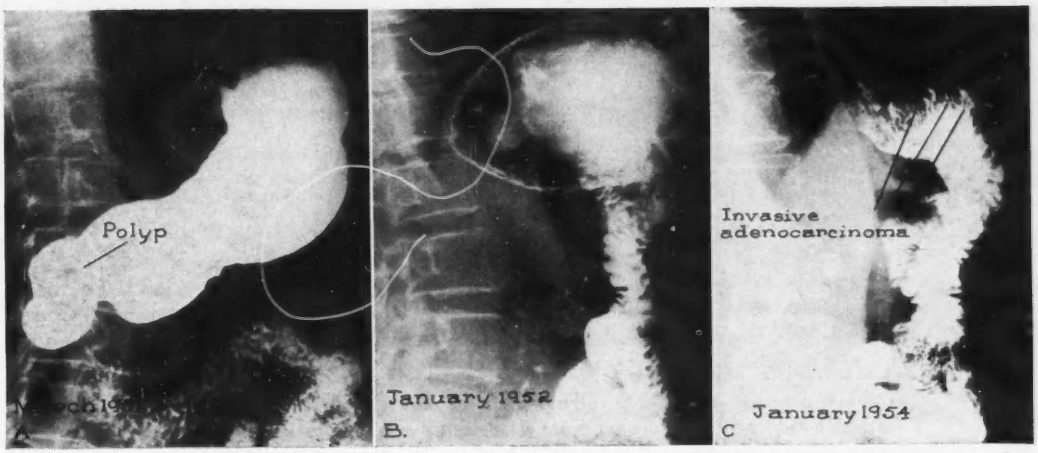

Figure 7.—Roentgen studies indicated a polyp in the prepyloric area. At operation a polyp high in the stomach (*A*) was electrocoagulated. Follow-up studies a year later showed no apparent disease. A well-functioning gastroenterostomy was present. (*B*) Obstructive symptoms developed three years after operation. (*C*) The entire gastric pouch was replaced by malignant disease.

symptoms were noted for the first time. She was observed at short intervals thereafter until March 1954, when x-ray evidence of stricture and the development of severe dysphagia led to emergency hospitalization. At operation March 11, 1954, a combined thoracoabdominal incision was made. A hard 10 cm. mass, which grossly was carcinomatous in character, was found in the residual stomach. It extended retroperitoneally into the region of the celiac axis and the aorta, and into the cardioesophageal junction. The remnant of stomach was removed and esophagojejunal anastomosis was done. Pathologic diagnosis indicated adenocarcinoma of the stomach with extension into the esophagus and jejunum with metastasis to lymph nodes.

The history and the subsequent course in the foregoing case strongly suggest that the third polyp which was present but not removed at the time of the first operation also contained adenocarcinoma and that it was not completely destroyed by the electrocauterization.

DISCUSSION

The three cases reported illustrate the malignant degeneration that may occur with nonoperative treatment. The author believes that in view of the degree of uncertainty inherent in all the diagnostic procedures now available, surgical removal is most likely to afford the patient the greatest degree of safety in most instances. It has been pointed out in several series reported in the literature that polyps tend to appear most often in the distal half or two-thirds of the stomach. In 21 of the 34 patients in the present series who were operated upon, the polyps were so located as to permit complete removal by either a Billroth I operation or subtotal gastric resection. In view of the malignant potential of these lesions, gastrectomy is probably the procedure of choice. However, as in this series wherein simple polypectomy was performed in 11 cases, wide local excision of the lesion with a generous segment of the gastric wall about the base of the polyp may be entirely adequate for single lesions. In such cases, however, immediate pathologic diagnosis of the excised specimen is necessary, and if malignant change exists gastric resection should be performed. Total gastrectomy was carried out in one of the two remaining patients treated operatively (both of whom had malignant change) while in the other the operative procedure was terminated after gastrostomy was performed to relieve cardioesophageal obstruction.

The author is of the opinion that if evidence of malignant change is present preoperatively and if many polyps involving the entire stomach are present at the time of operation, the principle of total gastric resection can logically be entertained. In an appreciable number of such cases, the continuity of the intestinal tract can be reestablished by simple esophagoduodenostomy or by the use of colon or jejunal segments to replace the excised stomach.

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The A.M.A. and Federal Legislation

TROUBLE, tragedy, and dissension are the major ingredients in the news today. Little attention is given to activities involving progress and agreement. Health legislation provides a good illustration of that point. During the past year or more the American public has become aware of the fact that the American Medical Association opposed the federal reinsurance proposal, disapproved of two provisions in the Social Security Act amendments, and disagreed with the government policy on medical care for veterans with nonservice-connected disabilities. Unfortunately, however, the public is not equally aware that during that same period of time the A.M.A. was giving active support to a large number of constructive legislative proposals involving medicine and health. We believe, therefore, that some long-overdue attention should be paid to the positive side of the record.

That record shows that the A.M.A. supported 11 of the 15 major medical bills that were enacted into law by the 83rd Congress. The Association opposed only two of the 15, and took no stand on the other two. The 11 proposals that the A.M.A. favored and which became public law were as follows:

Expansion of the Hill-Burton Hospital Construction Act to help finance the building of new nonprofit health facilities

Extension of the regular Hill-Burton Act to 1960

Lowering of the medical expense tax deduction from 5 per cent to 3 per cent

Extension of the "Doctor-Draft" law to 1955

Establishment of the Department of Health, Education, and Welfare

Establishment of the Hoover Commission on Organization of the Executive Branch of the Government

Establishment of the Commission on Intergovernmental Relations

Transfer of the Indian hospital and medical service from the Department of the Interior to the Public Health Service

Ban against the shipment of fireworks into states where their sale is illegal

A federal charter for the National Fund for Medical Education

Permission for oral narcotic prescriptions under certain conditions and limitations.

In addition to those 11 measures, the A.M.A. also supported two major proposals that were not acted on by the 83rd Congress. These were the administration bill to streamline Public Health Service grants to the states and the Jenkins-Keogh bills to stimulate the establishment of private pension plans by self-employed persons and by employees not covered by company plans.

We may be indulging in a bit of wishful thinking, but it would be helpful if the American people had more knowledge of the fact that the A.M.A. every year supports constructive legislation. The positive side of the story may not have blood-and-thunder news interest, but it spells out steady, continued progress in protecting the public health and welfare.

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Prostatic Carcinoma Involving the Rectum

The Problem of Differentiation from other Malignant Lesions

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• In a series of 150 cases of prostatic cancer, thirteen involved the rectum and presented the problem of differential diagnosis.

Although special studies were helpful, the resolution of the problem depended upon adequate biopsy for histological diagnosis. The treatment was palliative estrogen therapy and bilateral orchiectomy.

A DEFINITE CLINICAL and pathological diagnosis of carcinoma of the prostate is often reached with considerable difficulty. This is particularly true when the presenting symptoms or the palpable or visible lesion draw attention to an adjacent structure such as the anorectal canal, urinary bladder, seminal vesicles, bony pelvis, retroperitoneal space and embryonic remnants. The importance of the correct diagnosis is emphasized by the therapeutic and prognostic advances made in recent years for cancer of the prostate. Conversely, the results might be less favorable if the lesion were treated as arising from another source.

This article discusses the methods of differentiating carcinoma of the prostate involving the rectum from other malignant lesions.

INCIDENCE

The incidence of carcinoma of the prostate involving the rectum or other adjacent organs has not been determined, although carcinoma of the prostate is known to occur in about 20 per cent of men over 55 years of age and is the cause of death in about five per cent of white men over 50 years of age.[11]

In the present study reports of 13 cases of prostatic carcinoma involving the rectum were noted in reviewing the records of two general hospitals* for a period of 30 months. In the same period at these hospitals there were approximately 150 cases of prostatic cancer.

Young[29] noted that of approximately 800 cases of prostatic carcinoma, not over 12 involved the rectal mucosa. Jackson and Anderson[12] collected reports of 27 cases of rectal metastasis from carcinoma of the prostate in approximately eight years. Graves and Militzer[7] reported that in 81 cases of carcinoma of the prostate the rectal lumen was occluded in five. Kickham[15] reported that rectal invasion was noted in 12 of 132 cases of carcinoma of the prostate in which autopsy was done. Arnheim[1] reported perirectal invasion in 11 per cent of 176 cases of carcinoma of the prostate in which autopsy was done, but rectal invasion in only one case.

Since cancer of the prostate usually arises in the posterior lamella of the gland, the incidence might be even higher were it not for the double thickness of tough Denonvilliers fascia acting as a barrier between the prostate and rectum.

CLASSIFICATION OF LESIONS

Lazarus[16] classified carcinoma of the prostate involving the rectum into three categories: (1) Diffuse prostatopelvic mass occluding the rectal lumen by pressure, (2) intramural rectal tumor not involving the rectal mucosa, and (3) tumor extending through the entire rectal wall and into the rectal lumen as a fungating mass. Anderson and Jackson[12] had a similar classification: (1) Extrarectal carcinoma of the prostate occluding the rectal lumen and impeding a sigmoidoscope (52 per cent), (2) annular, stricturing, perirectal lesion due to prostatic carcinoma (7 per cent), and (3) carcinoma of the prostate invading the rectal mucosa with or without features of number one or two (41 per cent).

The author's classification, which adds a fourth category to the aforementioned three categories, is shown in Table 1 and illustrated in Figure 1.

TABLE 1.—*Classification of 13 cases of carcinoma of prostate involving the rectum*

Group	Number
1. Occluding rectal lumen	2
2. Annular, perirectal lesion	6
3. Invading rectal mucosa with or without features 1 and 2	3
4. Separate metastasis to rectosigmoid	2
Total	13

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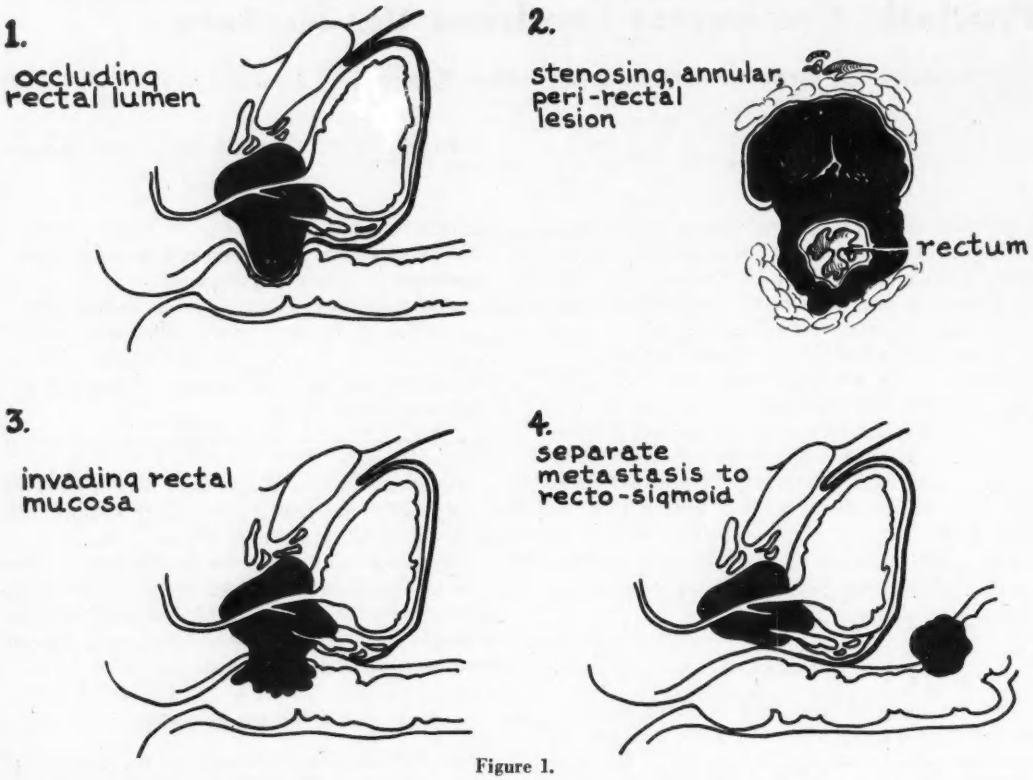

Figure 1.

METHODS OF MAKING DIAGNOSIS

The diagnosis of prostatic cancer should always be confirmed by adequate biopsy. Additional information may be obtained from determinations of serum phosphatase levels, from tissue assays for acid phosphatase activity, from cytological examination of the prostatic smear or urine sediment, from cystoscopy and sigmoidoscopy and from roentgenologic examination of the bones, lungs and occasionally the gastrointestinal tract.

Biopsy material may be obtained by a variety of methods which include transurethral resection, open perineal excision, open suprapubic operation, transrectal biopsy,[6] needle biopsy,[13] use of a Lowsley biopsy instrument and aspiration of bone marrow. No matter what method is used for the biopsy the emphasis is upon obtaining an adequate specimen and correct interpretation.

Serum acid phosphatase levels[28] may be abnormally elevated when prostatic cancer is invasive, usually in proportion to the extent of dissemination. An increase in acid phosphatase may also occur occasionally, however, after prostatic manipulation when malignant disease is not present, or in association with prostatitis, or when cancer originating elsewhere invades the prostate or adjacent structures. Laboratory error also is a possibility. The acid phosphatase levels may return to normal after metastatic carcinoma has been treated with estrogens and/or castration, and determining the content from time to time is thus an aid in evaluating the effectiveness of treatment. Recently Fishman and others[4] reported a new method for estimating serum acid phosphatase of "prostatic" origin in distinction from the older methods of estimating "total" body serum acid phosphatase. If confirmed by further clinical investigation, the sensitivity of this test may increase the value of acid phosphatase determinations in serologically diagnosing prostatic carcinoma.

Tissue assays[3] and special stains[5] with affinity for acid phosphatase in biopsied lesions will differentiate prostatic from other carcinomata in many instances. However, assays showing low content are more reliable as an indication of the absence of prostatic cancer than is a high assay as an indication that prostatic cancer is present.

Cytological study[21] of the prostatic secretion and urinary sediment may be helpful in diagnosing pros-

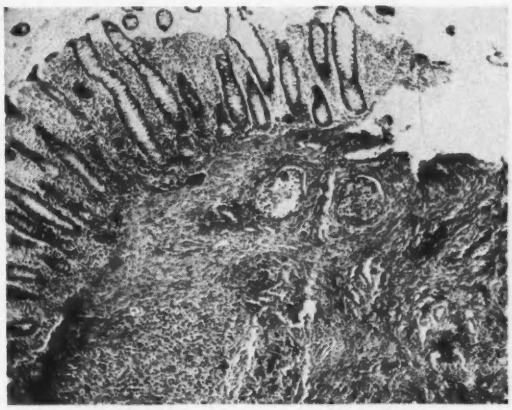

Figure 2.—Rectal biopsy (Case 1) showing normal rectal mucosa above and two nests of neoplastic cells in the middle (×80). Below are many tumor cells infiltrating from carcinoma of the prostate.

tatic cancer. The reliability of cytological interpretation varies with the experience of the interpreter.

Roentgenologic survey of the bones is of great value in diagnosing prostatic carcinoma that has metastasized but occasionally the roentgenologist is hard pressed to differentiate Paget's disease or other lesions of the bones. A diagnostic problem may be raised also if upper gastrointestinal roentgenograms may demonstrate a silent gastric tumor[24] that has produced a Blumer's rectal shelf. Roentgenograms of the colon may give helpful information in some circumstances.

The final diagnosis of prostatic neoplasm rests upon histologic examination of the biopsy specimen.

REPRESENTATIVE CASES

CASE 1. A 61-year-old white male was admitted to the hospital in October 1953 with chief complaint of pain in the back. In addition he had symptoms of dyspnea on exertion and had lost eight pounds of weight in recent weeks. He had a histological diagnosis of prostatic carcinoma following transurethral resection in 1951 with subsequent estrogen treatment. There was no roentgenological evidence of bony metastasis, although the serum acid phosphatase was 1.8 Bodansky units (normal is below 1.2) and alkaline phosphatase 8.8 Bodansky units (normal is below 3.9). Sigmoidoscopic examination beyond 7 centimeters was blocked by a cauliflower-like annular lesion involving the rectal mucosa (Group 3). This was outlined by barium enema. Needle biopsy of the prostate was reported again as adenocarcinoma, while biopsy of the rectal lesion was interpreted as adenocarcinoma of undetermined origin (Figure 2). Consultants in urology felt that the rectal lesion was prostatic carcinoma and recommended treatment of it as such. However, a surgical tumor board recommended abdominal exploration and probable abdominal-perineal operation for possible carcinoma of the rectum. Upon exploration a fixed pelvic mass with metastases to regional lymph nodes and liver was observed and sigmoid colostomy was performed. Exploration for postoperative bowel obstruction was carried out a week later and the patient died six weeks later of postoperative complication. Permission for autopsy could not be obtained.

This case illustrates how a presenting rectal lesion may be misinterpreted, although a definite histological diagnosis of prostatic cancer was available.

CASE 2. The patient, a 59-year-old white man, was admitted to the medical service of the hospital in July 1953 with complaint of lower abdominal cramps and scrotal swelling. Three months previously an inguinal node biopsy in another hospital revealed carcinoma of undetermined origin and deep irradiation to the pelvis was recommended. Results of intravenous urography, cystoscopy and upper gastrointestinal roentgen examination at that time were negative. Barium enema (Figure 3) showed an extrinsic defect in the rectosigmoid junction area and in three sigmoidoscopic examinations a constricting lesion was observed at the 15 centimeter level. The prostate felt nodular. No abnormality was noted in examination of a specimen taken by punch from the prostate, and serum acid phosphatase was within normal limits. The patient was transferred to the urological service in September 1953 where open perineal biopsy (Figure 3) of the prostate revealed adenocarcinoma. Castration was carried out and estrogen therapy was administered with satisfactory results.

CASE 3. A 62-year-old Negro male was admitted to the hospital, June 1953, with complaint of left upper abdominal pain, relieved by eating. A small, irregular, hard mass was felt overlying the prostate and involving the rectal mucosa. Blood was observed on the glove used in rectal examination. Acute and chronic inflammatory changes were observed in biopsy of rectal tissue, and a second biopsy (Figure 3) was interpreted as adenocarcinoma of undetermined origin. Roentgenograms of the colon (Figure 3) showed a rectal lesion. In upper gastrointestinal roentgenograms a duodenal ulcer was noted. There were questionable osteoblastic metastatic bone lesions. Serum acid phosphatase was 40 units (normal 0 to 1.1 Shinowara units) and serum alkaline phosphatase, 10 units (normal 2 to 4.5 Shinowara units). Needle biopsy of the prostate showed primary adenocarcinoma. The patient declined castration and was treated with estrogen with good results.

This case is illustrative of the difficulty of differentiating prostatic from rectal carcinoma.

SUSPECTED CARCINOMA OF PROSTATE NOT INVOLVING RECTUM

The following case is not included in the series (Table 1) but illustrates the problem of obtaining histological evidence of carcinoma of the prostate.

CASE 4. A 64-year-old white male was admitted to the orthopedic service of the hospital in February

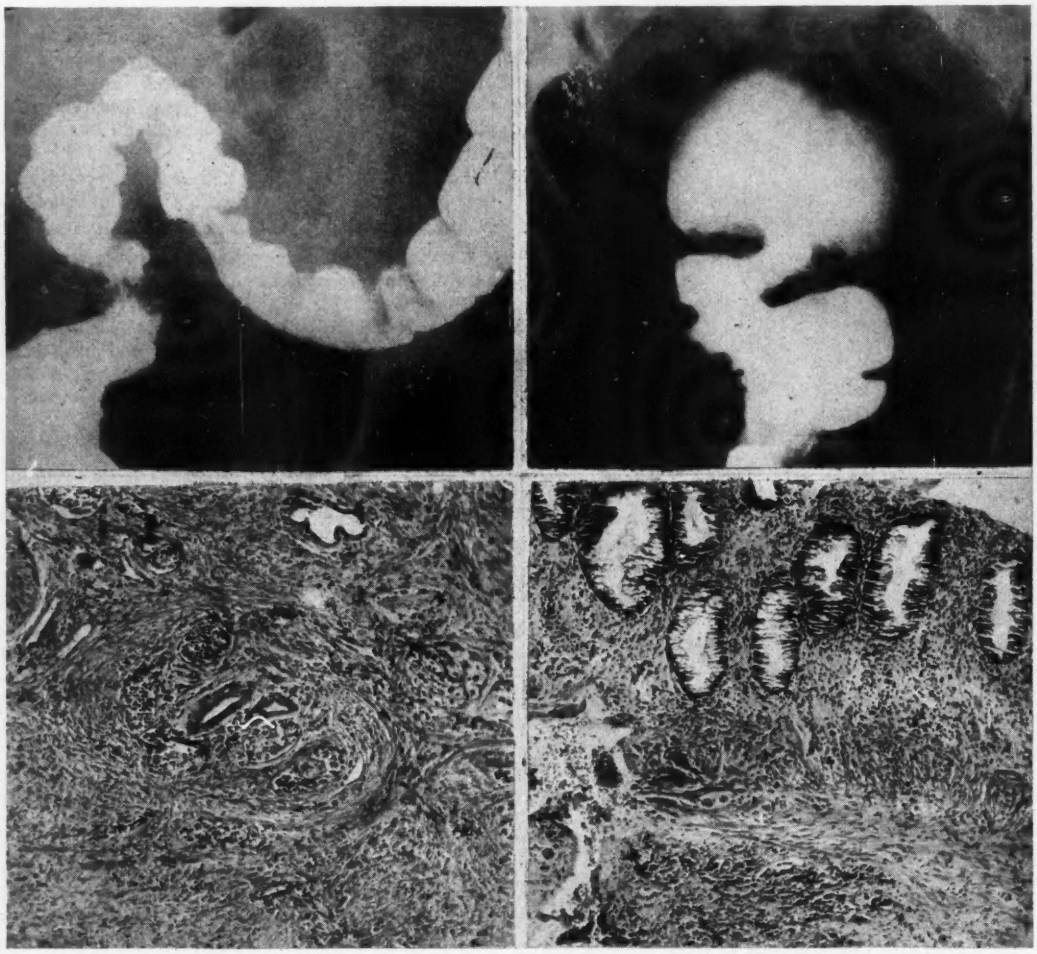

Figure 3—*Upper left* (Case 2)—Barium enema showing constricting rectal lesion from carcinoma of the prostate.

Lower left (Case 2)—Open perineal biopsy (×80) of prostate showing nests of prostatic carcinoma cells in lymphatic spaces near center. These surround two vessels.

Upper right (Case 3)—Barium enema shows rectal lesion produced by prostatic carcinoma.

Lower right (Case 3)—Rectal biopsy (×80) showing rectal mucosa above and neoplastic cells below in the muscular tissue having characteristics of adenocarcinoma.

1954 with chief complaint of low back pain that had been incapacitating for four months. There were no outstanding complaints referable to the genitourinary system, but upon rectal examination the prostate was noted to be enlarged, irregular, hard and fixed. The residual urine in the bladder was found to vary between 50 and 90 cc. Osteoblastic metastatic bone lesions of the pelvis and vertebrae were noted in roentgenograms. Serum acid phosphatase levels were normal on four occasions. Clinically this case was one of carcinoma of the prostate with bone metastasis. However, material removed from two sites by Silverman needle and tissue excised in extensive transurethral resection of the prostate revealed no carcinoma. Finally, a transrectal biopsy of the prostate showed definite adenocarcinoma present in the posterior palpable portion of the gland. The rectal wound healed without complication. Orchiectomy was carried out and estrogen therapy was administered. In this case transrectal biopsy of the prostate was found to be technically simple, the exposure excellent, and the operation one of short duration and without complication.

CARCINOMA OF URINARY BLADDER INVOLVING RECTUM AND SIMULATING CANCER OF PROSTATE OR RECTUM

The following case also was not included in Table 1 since it represents carcinoma of the urinary bladder simulating prostatic or rectal carcinoma, but it illustrates the diagnostic problem that arises. Four such cases were observed in a period of six months.

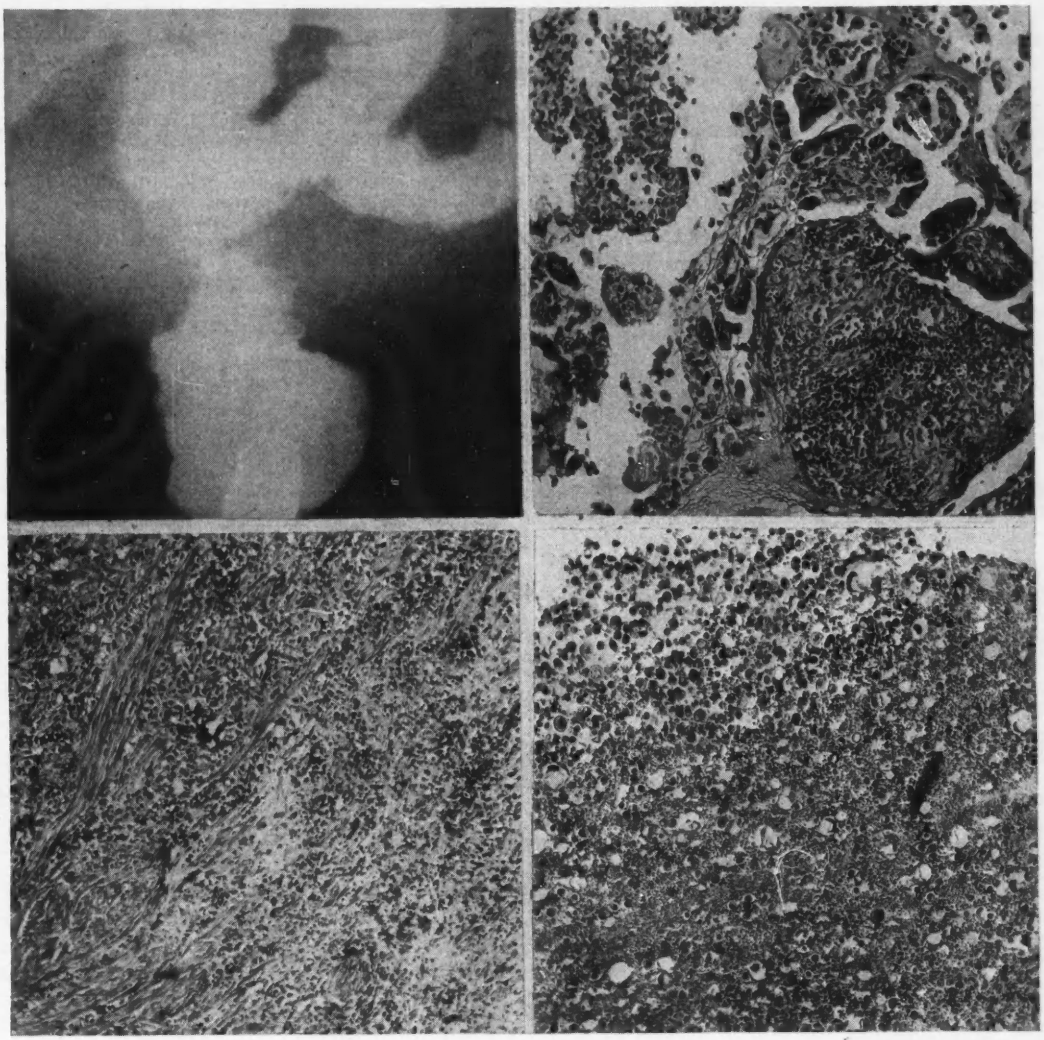

Figure 4—*Upper left* (Case 5)—Barium enema showing rectal lesion due to carcinoma of the urinary bladder.
Upper right—Bladder biopsy (×125) showing highly malignant epithelial tumor exhibiting signet cell simplex features.
Lower left—Needle biopsy (×80) of prostate showing infiltration with highly malignant tumor.
Lower right—Cellular pattern of the ascitic fluid showing many signet cells from bladder carcinoma (×250).

CASE 5. A 69-year-old white man was admitted to the medical service of the hospital with chief complaints of lower abdominal discomfort, abdominal enlargement and decreased caliber of stools. The patient also had gross hematuria for two weeks before admission. Upon physical examination an abdominal fluid wave was noted and a large anterior rectal-pelvic mass simulating Blumer's shelf was palpated. Carcinoma of the prostate and carcinoma of the urinary bladder were considered the most likely diagnoses. Serum acid phosphatase levels were normal on two occasions and thrice normal on a third. There were no bone lesions. The rectal mass impeded sigmoidoscopy and was outlined by barium (Figure 4). Neoplasm was not seen in biopsy of the rectal mucosa or in tissue taken by Silverman needle from the prostate. Upper gastrointestinal roentgenograms and gallbladder series were normal. Cystoscopy revealed marked infiltration of the mucosa of the floor with multiple papillary tumors. The bladder biopsy as reported by the pathologist was: ". . . highly malignant epithelial tumor exhibiting signet cell simplex features (mucin secreting) (Figure 4). This unusual neoplasm, if derived from bladder or adjacent structures, certainly represents an unique primary neoplasm. It is, however, quite possible. One must

rule out extension of neoplasia from the gastrointestinal tract." A repeat prostatic needle biopsy (Figure 4) as well as examination of ascitic fluid (Figure 4) revealed similar neoplastic cells. The patient expired January 1954 and autopsy revealed primary bladder tumor with no gastrointestinal lesions other than metastasis to the rectum.

TREATMENT

Once carcinoma involving the rectum has been diagnosed as prostatic in origin, appropriate treatment should begin. It is incurable in advanced state and palliation is brought about by a combination of medical and surgical therapy. Radical pelvic operation does not seem indicated, nor does colostomy appear in order for rectal obstruction. The combination of castration and estrogen therapy[9, 19] is most effective.

Recent experimental studies[2, 22] suggest other forms of palliation: injection of radioactive isotopes,[14, 18] total adrenalectomy,[10, 27] cortisone to produce medical adrenalectomy,[26] hypophysectomy[17, 25] and/or hypophyseal irradiation[19] and intravenous conjugated estrogens.[23] These methods have yet to be adequately evaluated in the treatment of prostatic carcinoma.

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Cholinesterase Inhibiting Insecticides (Parathion)

Chemical and Clinical Aspects

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• *Since parathion and other cholinesterase insecticides are being used extensively, safety precautions are important, and the need for prompt and adequate therapy if poisoning does occur must be emphasized.*

This paper stresses the acute nature of the poisoning and attempts to outline the basic principles of therapy so that practicing physicians may handle cases with more confidence, which should help prevent prolonged periods of functional disturbances due to anxiety following poisoning.

THE GROUP OF PHOSPHATE ESTERS which are cholinesterase inhibiting agents was discovered in the Cambridge laboratories of Sir Henry Dale in 1941. The original anticholinesterase substances were primarily only of pharmacologic interest. However, during World War II German chemists working to develop a "nerve gas" discovered several new substances of the "organic phosphate" series which were very active cholinesterase inhibitors and extremely toxic to man. The formulae of these substances were discovered by a team of chemists investigating captured chemical data. The first, HETP (hexaethyltetraphosphate) which broke down into the active substance TEPP (tetraethylpyrophosphate), was found to be effective for agricultural use but was too unstable to be practical. Finally, parathion (O, O, P-nitrophenylthiophosphate) was discovered to be both effective and stable.

These substances possess important qualities not found in other insecticides. When they are applied to the plant in the form of dust or water-soluble spray (in a dilution of .02 to .08 per cent), the active substance (parathion) is hydrolized and absorbed into the plant, so that insects are actually poisoned by eating the leaves or juices of the plant and not necessarily by contact or incidental ingestion of surface chemicals. These substances remain in the plant tissues for a variable length of time. Tracer studies with radioactive phosphorus (P^{32}) by Hartley and Heath[13] show that all but 10 per cent of the absorbed parathion is usually decomposed in living plants after four weeks. However, the rate of decomposition depends on the species, the rate of growth, the air temperature and the part of the plant studied.

Experiments by Payton[16] and Aldridge[2] in vitro revealed that chemically pure parathion has very little, if any, anticholinesterase activity, but that after ultraviolet exposure or hydrolysis it becomes an active anticholinesterase. Myers and Mendel[15] observed that it is extremely difficult to test the toxicity of these substances because impurities or decomposition products in vivo may produce substrates that are many times more toxic than the original chemical.

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These studies lead to conjecture that pure parathion may not be toxic, but may become an anticholinesterase agent after absorption and reaction brought about by various enzyme systems, both in plants and animals. It is this observation that leads chemists to believe that a new and safer insecticide of this series may be discovered. Such a substance might be transformed into a toxic substrate by enzyme systems found in insects but not in warm-blooded animals. Thus insects would produce their own poison from a harmless precursor substance. Such a substance obviously is not yet known.

According to Wong[21] there are four enzymes which may be affected by anticholinesterase: true cholinesterase, pseudo-cholinesterase, ali-esterase and lipase. Since these four enzymes may be affected by the anticholinesterase; and since the degree of activity depends more upon hydrolysis and products than on the pure chemical; and since the nature of the hydrolysis end products is not yet known; and since the hydrolysis end products act on one or all the known anticholinesterase enzymes, probably at different rates of speed, the complexity of the problem becomes obvious. This complexity is magnified by the fact that the hydrolytic products may be 40 or 50 times more toxic than the original substance. Consequently, a trace of such substances would cause wide variation in results.

CLINICAL FEATURES

For simplicity let it be assumed that parathion acts directly on cholinesterase and that this in turn allows toxic quantities of acetylcholine to collect in

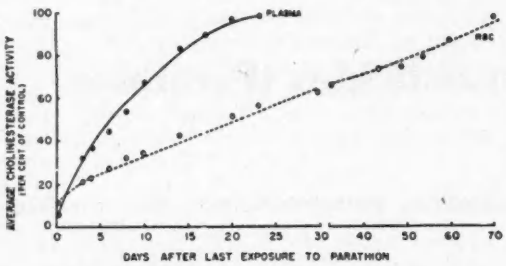

CHART 1.—Recovery of plasma and erythrocyte cholinesterase activity after cessation of exposure to parathion—average values obtained in 18 subjects. (From Grob, Garlick and Harvey.)

the tissues and produce symptoms of acetylcholine or mecholyl poisoning. These symptoms may be classified into three groups:

1. *Muscarine-like effects:* The acetylcholine effect on postganglionic cholinergic nerves is characteristic of muscarine poisoning. This group of symptoms is first to appear and is heralded by anorexia and nausea, soon followed by abdominal cramps, vomiting, sweating, salivation and pupillary constriction. As the poisoning becomes more intense tenesmus and diarrhea appear, sometimes associated with involuntary defecation and urination. Pinpoint nonreactive pupils, blurred vision, respiratory distress and excessive bronchial secretions ensue, followed by pulmonary edema and cyanosis. Elevation of blood pressure is frequently noted in severe parathion poisoning. Gastrointestinal symptoms may be more prominent when the poison is ingested or absorbed through the skin, and the respiratory symptoms more severe when the poison is inhaled.

2. *Nicotine-like effects:* The preganglionic and somatic motor nervous systems are affected in such a way as to simulate nicotine poisoning. This is characterized by fasciculation of the muscles, first of the iris and tongue, later of the face, neck and extraocular group, and finally by generalized muscular fasciculations and weakness. In severe cases the weakness may involve the muscles or respiration.

3. *Central nervous system effect:* Restlessness, anxiety, tremor, ataxia, dizziness, sleepiness, paresthesias, mental confusion, disorientation, excessive dreaming, coma and generalized convulsions occur as the result of central nervous system poisoning.

Any person or groups of persons who are working with insect sprays or "nerve gas" and who have these symptoms should be considered to be suffering from acetylcholine poisoning until proved otherwise. Verification of the diagnosis may be made by taking blood tests for cholinesterase activity. Such tests, which are done by commercial or state laboratories in most regions of the country, are of utmost importance in the diagnosis of subclinical cases and in the observation of employees known to be working in the presence of parathion. However, in persons with symptoms suggestive of parathion poisoning, treatment should be instituted at once without waiting for the confirmatory laboratory tests.

Chart 1 (after Grob, Garlick and Harvey) shows the average cholinesterase activity in 18 normal persons after parathion intoxication. From this group it is apparent that the plasma level returns to normal after about 15 to 20 days, and erythrocyte level in 60 or 70 days. This is said to be due to the formation of new cholinesterase within the body and does not indicate the detoxification of poisoned cholinesterase.

Poisoning with parathion is, as a rule, acute although exposure of a person to small doses over a long period of time may bring about a pronounced decrease in cholinesterase which in turn reduces the tolerance for parathion so that acute parathion poisoning may develop with a relatively small amount of the poison. This could be prevented by periodic blood cholinesterase tests on persons working with parathion.

In addition to actual acetylcholine poisoning, the possibility of aggravating some disease which is known to be in some way related to increased parasympathetic activities, must be considered. Such diseases include bronchial asthma, Parkinsonism, duodenal ulcer and ulcerative colitis.[20]

TREATMENT

The treatment of parathion poisoning is simple but should be carried out promptly and the patient should be kept under continuous observation until he is out of danger.[22] Atropine is the lifesaving antidote, and it should be administered at once, without delay for transporting the patient to a hospital. An initial dose of 2 mg. should be administered hypodermically, and that amount should be repeated at short intervals until dryness of the mouth and symptoms of myosis are produced. Also of immediate importance is the removal from the skin, hair and stomach all clothing and foreign substances that might contain parathion. It is important to bear in mind that since parathion is absorbed through the skin, physicians and others dealing with a patient must take care in the removal of contaminated clothing lest they also become poisoned. The "cleaning up" procedure would best be carried out in the open, so that rooms, beds, ambulances and other equipment will not become contaminated. In addition to the two primary therapeutic measures of administration of atropine and removal of the patient from further contact with parathion, artificial respiration may be necessary in cases of respiratory paralysis, and various forms of symptomatic treatment may be indicated in individual cases. Hamblin[10] pointed out

that a readily accessible supply of atropine with the proper directions for emergency use is just as important for the safety of persons handling phosphate esters as a fire extinguisher on a boat is for the safety of the crew.

The use of magnesium sulfate intravenously has been suggested to counteract muscular excitability (nicotine effect). However, it was pointed out by Hanzlik[12] that in the event of parathion poisoning in which atropine did not arrest muscular excitability, the poisoning would be so profound that large, nearly toxic doses of magnesium would be required and that the risk of cardiac failure or of respiratory failure due to magnesium might contraindicate its use. Neither blood transfusion nor the administration of concentrated cholinesterase has proved effective in the treatment of parathion poisoning. As was pointed out by Hamblin,[10, 11] the molecular weight of cholinesterase is approximately 400,000 and that of parathion is 323. Consequently it would require 1.2 grams of cholinesterase to neutralize each milligram of parathion. General supportive measures, such as postural drainage in the case of excessive mucus in the bronchi and oxygen therapy in cases of cyanosis are indicated.

Specific precautions should be taken to discourage prophylactic use of atropine, as it is obvious that anyone taking atropine before risking exposure to parathion may thereby deprive himself of the warning symptoms which might otherwise permit the timely application of therapeutic measures.

The duration of acute parathion poisoning is from two to four days, and (as noted in Chart 1) after a period of 30 to 60 days the bodily stores of cholinesterase will have been completely replaced and the patient will consequently be completely recovered from poisoning without residual effect.

It should be stressed that physicians should deal calmly and in reassuring manner with patients who have parathion poisoning. Due to the effect of this drug on the nervous system, patients become suggestible. In one of the cases observed by the author, the first physician to treat the patient was said to have thrown up his hands and said, "You have been severely poisoned; I don't know what to do for you." Such uncertainty and indication of serious poisoning magnifies fear in an already terrified patient and conjures visions of poisoning with permanent residual disability. In these circumstances the patient is likely to become neurotic and may develop functional symptoms which persist for months or years. Symptoms of this kind are frequently nurtured by well-meaning legal advisors. Following are reports of four cases in point.

REPORT OF FOUR CASES

CASE 1. The patient was one of a group of 20 men poisoned with parathion in a pear orchard (the incident was reported by Abrams[1] in 1950). All the men were promptly and adequately treated with atropine and all but one recovered within four days without residual effect. The one who had continuing effect, the patient in the present case, was Mexican who did not understand English well. He was first observed by the author ten weeks after the exposure to parathion, and at that time said he felt weak and tired and had constant frontal headache and recurrent epigastric distress. On physical examination tenderness was noted in the upper midabdomen. The liver was normal in size, and there was no abnormality in the reflexes or in the reaction of the pupils. Pronounced cardiospasm, pylorospasm and spasticity of the colon were noted in roentgen studies. The patient had not returned to work and was not exposed again. The blood level of cholinesterase was normal. The patient had a poor work history; in fact, the day that he was poisoned was his first day at work for several weeks. It was concluded that the symptoms were due to a functional disturbance of the gastrointestinal tract and that it was doubtful that cardiospasm, pylorospasm and spasticity of the colon were related to exposure to parathion. However, it is conceivable that such functional conditions could have been aggravated for a short time following exposure to parathion.

CASE 2. The patient complained of various and bizarre symptoms over the preceding two years and volunteered the information that sprays, particularly parathion, caused the pupils of his eyes to become small, and that he occasionally felt dizzy. He was mechanic and repairman on airplane spray rigs, which involved welding metals that had been contaminated by sprays. The patient said that "potent vapors" arose from the heated metals. His chest, he said, felt "choked up" and, in view of this symptom he had discontinued working for the past two months without relief. Upon examination, bronchial asthma with 4 per cent eosinophilia was noted. Cholinesterase activity in both the plasma and the erythrocytes was within normal limits. The patient was anxious and introspective about his health and was fearful of having been fatally poisoned. That he had allergic sensitivity to some substance in the sprays is possible, and it is conceivable that he had some mild symptoms of parathion intoxication from time to time. In view of the continued symptoms even after two months away from work and the fact that the blood cholinesterase was normal, it was concluded that the chief difficulty was bronchial asthma and that parathion played no part in the symptoms noted at the time of examination. Reassurance that all ill effects of parathion were gone greatly relieved the patient's anxiety and symptoms.

CASE 3. The patient was first observed by the author seven months after an acute illness that was characteristic of moderately severe parathion poisoning. At the time of that illness he was employed as a marker to put down flags in a cotton field that was being dusted from the air with a powder containing parathion. He noted general "nervous trem-

TABLE 1.—*Reported deaths due to parathion*

Case	Source	Occupation	Exposure	Comments
1.	American Cyanamid Co. circular letter May 12, 1949	Foreman in spray manufacturing plant	Splashed 95% parathion on arms at 3 a.m. Cleansing not properly carried out.	Fellow worker similarly exposed but who carried out cleansing promptly was not ill. Patient's symptoms started at 11 a.m. He first saw a doctor at 6:30 p.m. and died at 12:20 a.m. Treatment probably not adequate.
2.	Abrams—1950 American Cyanamid Co. Communication 1949	Employed by Agricultural Experiment Station	Sprayed for several hours in clothes soaked in weak parathion solution	Patient disregarded safety precautions and did not attempt to decontaminate self after known exposure. He did not see a doctor.
3.	Grob & Garlick 1949	Chemical plant worker	Mixing liquid parathion and dust to make "wettable mixture"	Inadequate protection. Death 10 hours after onset of symptoms. Autopsy showed general hyperemia and "pressure cone" at base of brain which may been the terminal cause of respiratory failure.
4.	Hamblin 1951 Case No. 1	Farm worker—illiterate; had not been properly cautioned	Walked behind mule-drawn sprayer and was soaked by spray	Patient was unaware of necessary precautions, so none was taken. No treatment.
5.	Hamblin 1951 Case No. 2	Filled citrus sprayer tanks	Skin wet by diluted spray. Had previously been poisoned 25 days prior to fatal accident.	Onset symptoms 10:30 a.m. Death 5:30 p.m. He did not take proper precautions.
6.	Johnston 1953	Child, age 9 months	Played with DDT parathion paste found in farm house. Found on skin and in mouth.	Patient was washed but not adequately decontaminated. Exposed at noon and symptoms did not appear until 5:30 p.m., at which time doctor was first called. Dead at 8 p.m.

ors," nausea, vomiting and severe "stomach cramps." He was admitted to hospital but a day passed before specific medication was begun. Atropine then was given for a period of two weeks. The patient said that the physician who treated him at the time said, "You have been severely poisoned; I don't know what to do for you." The patient was apprehensive and seemed certain that some irreparable damage had been done. He said that after recovery from the acute episode he felt weak and tired, had palpitation of the heart and epigastric distress, and became so fatigued that he could not return to work.

Upon physical examination upper midabdominal tenderness was noted and roentgen studies revealed a duodenal ulcer, but there were no other abnormal objective findings. Results of blood cholinesterase studies were normal. It was concluded that the patient had had a mild degree of parathion poisoning which was complicated by duodenal ulcer. That the ulcer occurred at the time of exposure to parathion was considered a possibility, but it was believed that once the original ulcer was healed, there should be no further residual organic effect from the exposure to parathion.

CASE 4. The patient was examined because of complaint of constant shortness of breath and pain in the chest and of cough and palpitation, which he said had begun some three months earlier when he was exposed to inhalation and dermal absorption of parathion while pulling a sprayer in which a water-soluble dust was mixed with water and was sprayed upon fruit trees.

Upon examination, a hiatal hernia, pylorospasm, and arteriosclerotic heart disease with bundle branch block were noted.

As there was a certain degree of functional overlay, the history was difficult to evaluate. The patient suggested that he was so short of breath that he could not walk one block to a streetcar from the hospital, yet the following day he asked permission to leave the hospital to go deer hunting.

It is probable that the patient had had mild parathion poisoning, but it is unlikely that the other demonstrable organic disease processes were affected by the exposure to parathion. It cannot be said with certainty, however, that the patient did or did not have coronary occlusion at the time of exposure.

PREVENTION

The manufacture and sale of parathion is carefully controlled by the American Cyanamid Company. The substance is sold only to special commercial jobbers, who are required to follow strict safety rules, and who require farmers who buy to follow strict precautions. If workmen follow the rules carefully, they will be in no more danger using parathion than any other insecticide. As a further precaution, it is wise to take periodic blood cholinesterase determinations to detect subclinical poisoning which may have resulted in some undetected breakdown in discipline.

Despite its great toxicity, there have been only six deaths reportedly due to parathion. Table 1 summarizes the six cases. (Not included are deaths of airplane pilots who have died as a result of crashes during the use of parathion. Such deaths may have been due to myosis or nervous changes brought about by exposure to parathion.)

There have undoubtedly been innumerable cases of mild and severe poisoning in which the patients recovered. It is noteworthy that all deaths listed in Table 1 occurred as a result of carelessness—either disregard of known rules and warnings, or insufficient instruction. Parathion poisoning is less frequent now than it was five years ago when proper treatment was not so well known and agricultural workers tended to hold warnings of toxicity in contempt. Now that the toxicity of parathion is appreciated, farm workers handle it with more respect.

OTHER ASPECTS OF PARATHION

In a review of the literature some interesting collateral observations with regard to parathion were noted. Grob[7] discussed the use of parathion in relationship to the diagnosis and treatment of myasthenia gravis. Annis[3] pointed out interesting electrolyte changes which occurred during the acute stage of one case of parathion poisoning. These changes include a reversal of the calcium phosphorus ratio in the blood, a marked increase in blood potassium level, and a marked decrease in the serum pH. These findings were observed in only one case and are admittedly meager observations, but may stimulate further observation of blood chemistry in acute parathion poisoning.

Sherwood[19] suggested that acetylcholine may be a factor in certain psychotic syndromes. He pointed out that acetylcholine aggravates Parkinsonism, as opposed to atropine which relieves these symptoms. In experimental work with cats he found that catatonic states were aggravated by intraventricular injections of acetylcholine, and that cholinesterase caused a temporary remission. He observed that certain anticholinesterase substances, (di-isofleurophosphonate) will, in toxic doses, cause a syndrome resembling schizophrenia, and will aggravate known schizophrenic symptoms. This may indicate another possible toxic reaction to parathion as yet unreported.

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Shigella Infections

Observations on Recognition and Management

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• In review of 117 cases of Shigella enteritis observed in the isolation division of the San Francisco Hospital, it was noted that the most common symptoms were high fever, liquid and bloody stools, prostration, irritability and meningismus. The use of antibiotics did not significantly affect the course of the acute illness but resulted in earlier elimination of the Shigella organisms from the bowel. "Carriers" were found to be particularly resistant to antibiotic therapy.

The disease is self-limited. In 30 cases the patients recovered with only symptomatic treatment. Management of fluid and electrolyte balance was often an important factor in supportive therapy.

DIARRHEA is one of the most common complaints in pediatric practice. There are, etiologically, many kinds, among them metabolic diarrhea, parenteral diarrhea, the nonspecific epidemic diarrhea and vomiting generally thought to be due to a viral infection, and, finally, enteric infections due to specific organisms and parasites such as Shigella, Salmonella and Endameba.

Shigella infections typically are characterized by a sudden onset of high fever, explosive diarrhea with liquid foul-smelling stools containing blood, pus and mucus, and pronounced prostration and irritability. Meningismus is also a common feature. Fever and symptoms of toxicity frequently precede the onset of liquid stools by several hours. Abdominal cramps and tenesmus, which are the most common symptoms in adults, are less frequently noted in children. Prostration is usually out of proportion to the amount of diarrhea and degree of dehydration. Multiple cases in a family should arouse suspicion of a specific enteric infection.

A very useful adjunct in diagnosis is examination of the liquid stool under the microscope. The presence of large numbers of erythrocytes and leukocytes is suggestive of Shigella infection. Definitive diagnosis is made by cultures of the liquid stool or by culture of material swabbed from the rectal mucosa. Explosive diarrhea and acute illness do not occur in all cases of Shigella enteritis. In a small number the symptoms are milder. It was noted by the author that recurrence or reinfection was less often accompanied by severe toxicity and high fever than the initial infection. Routine cultures of specimens taken from persons in the same household as a patient are likely to reveal a number of carriers of the organism.

Shigella dysentery is generally considered to be an epidemic disease, particularly likely to occur during war or famine and in crowded institutions and orphanages. However, in addition it is often found to occur endemically in the more crowded areas and to infect family groups. Felsen[2, 3] recently stressed the high incidence of Shigella infections. An impressive number of cases have been observed in recent years in the emergency room and the out-patient clinic of the San Francisco Hospital.

Although the diagnosis can readily be made clinically, the proof rests with the demonstration of the organism on stool culture. Thus, the reported incidence of the disease depends to a very great degree on how many cultures are taken. In the author's experience the reported incidence always rose considerably when the house staff's index of suspicion was high.

For the 12 months ended June 30, 1950, 1,005 cases of Shigella dysentery were reported in California, with 24 deaths. This compared with 413 cases of Salmonella infection and 325 cases of amebiasis for the same period. In the 12 months to June 30, 1951, 585 cases of Shigella dysentery were reported, with 14 deaths; and in the same period there were 476 cases of Salmonella infection and 377 cases of amebiasis.

There is little doubt that the true incidence of Shigella enteritis is considerably higher. In some instances the diagnosis is not suspected; more frequently, although it is suspected and the patient treated, no cultures are taken and the diagnosis is not made definitively. Since this is a communicable disease, particularly within family units, it is important that it be diagnosed and managed in such a way as to minimize the spread of pathogens within the family unit and within the community.

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The terramycin and polymyxin used in the cases reported upon were supplied by Chas. E. Pfizer Company of Brooklyn, N. Y.

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TABLE 1.—*Symptoms of 95 acute cases at the time of admission to hospital*

	No. of Cases	Per Cent
Fever over 100° F. rectally	88	84
Fever over 104° F. rectally	40	38
Liquid stool	91	86
Bloody stool	44	42
Pronounced lethargy	46	44
Pronounced irritability	23	22
Meningismus	28	27
Moderate to severe dehydration	57	54

The purpose of this presentation is to call attention to the considerable incidence of Shigella enteritis in endemic form, and to make several observations concerning recognition and management. To this end, the records of the isolation ward of San Francisco Hospital between August 1950 and August 1953 were reviewed.

REVIEW OF CASES

One hundred seventeen patients with Shigella enteritis were admitted during the three years. Ninety-five of them were acutely ill and 22 were carriers. Seventy-eight of the cases were caused by Shigella sonnei, 23 by Shigella of the Flexner type, and 17 by other Shigella organisms, among which were Shigella alkalescens, Shigella dispar and Shigella boydii. It is interesting that not a single case of Shigella dysenteriae was encountered. There was no statistical relationship between the kind of organism and the severity of disease. Only four of the 117 patients were adults, two of whom were student nurses who were exposed to infection on the ward. Of the 113 children, 95 were between the ages of one and five years; seven were between three months and one year; the rest were between five and 15 years. A factor in this age distribution probably was that the criteria used for hospital admission were severe diarrhea with dehydration, or the presence of severe toxicity. Dehydration tended to be more pronounced in the younger age group. Many additional patients observed in the emergency room and out-patient clinic were thought, on the basis of clinical symptoms, to have Shigella infection but were considered not sick enough to require hospitalization.

Symptoms in the 95 acute cases at the time the patient was admitted are listed in Table 1. Fever, liquid and bloody stools, pronounced lethargy and irritability were the most common. Meningismus was present in 26 per cent of the cases and in half it was so pronounced that lumbar puncture was done upon admission. The number of stools per day was quite variable and, in the author's opinion, the most unreliable feature in the history. There was very little correlation between the number of stools (as reported by the mother) and the presence of severe dehydration. There was one death in the series: a severely dehydrated child died 20 minutes after admission.

Many different kinds of therapeutic regimen were used. The records were reviewed to determine any differences in the clinical response to the variety of therapeutic agents. The selection of the antibiotic or sulfa drugs to be used for any particular patient was at the discretion of the resident on the ward.

One group of 30 cases in which only symptomatic therapy was given was composed of cases where a decision was made at the time of admission to use no therapy until the organism was identified by the laboratory. Then, when a report on the culture was made two to three days later, the patient was sufficiently improved in most instances and was continued on symptomatic therapy only.

The distribution of the severely ill and mildly ill children, as well as Flexner and sonnei type of Shigella, were generally comparable in the different treatment groups. Drugs were started on the first to fourth day of the disease and were continued for six to seven days, and as long as ten days in some instances. Terramycin and chloramphenicol were used in a dose of 50 to 60 mg. per kilogram of body weight, given orally; neomycin 1.5 to 2.5 gm. daily, by mouth; sulfadiazine 125 mg. per kilogram of body weight, by mouth; polymyxin 200 to 300 mg. daily, by mouth; aureomycin 35 mg. per kilogram of body weight, by mouth.

The kinds of treatment and the results are summarized in Table 2. "Duration of positive stools" as shown in the table was the length of time from admission until the first culture negative for Shigella was obtained. In this regard it should be noted that in most cases stools were not examined bacteriologically while treatment was being given. Examinations were resumed on the last day of therapy. This accounts for the fact that none of the periods was less than a week. Duration of hospital stay was determined by the City of San Francisco requirement that three negative stool cultures be obtained before discharge of the patient from the hospital.

The results as shown in Table 2 bring out the fact that Shigella enteritis is a self-limited disease. Thirty patients recovered satisfactorily with symptomatic therapy only. It was interesting that the clinical course as measured by the duration of fever and of diarrhea was not influenced by the administration of any one of the antibiotics. However, the length of time during which the stools remained positive was definitely cut down by the use of broad spectrum antibiotics and sulfadiazine. This shortened the hospital stay of the patient, as indicated.

Neomycin was tried on 13 patients and, as is clearly brought out in the accompanying table, a good many bacteriological failures were encountered. It did not exert any significant influence on

TABLE 2.—*Results of treatment of acute Shigella enteritis in 95 acute cases*

Treatment	Number of Patients	*Failure of Treatment	Duration (in days) of— †Fever	‡Abnormal Stools	Positive Stools	Hospital Stay (days)
Symptomatic only	30	0	2.2	4.0	13.0	21.6
Terramycin (acute cases; treatment started first or second day)	27	1	2.1	3.6	9.3	15.7
Terramycin (treatment started between twelfth and fortieth day)	5	1	2.0	3.4	32.6	40.0
Neomycin	13	4	1.9	8.6	19.0	22.4
Sulfadiazine	8	2	2.3	4.0	10.0	16.0
Chloramphenicol	6	0	2.0	5.0	8.0	13.0
Polymyxin	2	1	2.0	3.5	11.0	18.0
Aureomycin	2	0	2.0	2.0	6.0	16.0
Aureomycin and sulfadiazine	2	0	1.5	6.0	13.0	18.0

*These are cases in which culture of stools was positive for Shigella after a seven-day course of treatment.
†Rectal temperature above 100° F.
‡Liquid and bloody and containing large amounts of pus and mucus.

the course of the disease, and its use was discontinued for that reason.

In the 22 carriers (not included in Table 2) the disease was more resistant to therapy than it was in the acute cases. Eight of these 22 carriers were treated with multiple courses of drugs; four of them were treated with terramycin and the stools remained positive for Shigella. They were retreated with a combination of terramycin and polymyxin for one week. Three of the four then had negative cultures and one continued positive but finally became negative after treatment with chloramphenicol for one week. The hospital stay in the latter case was 39 days. Another carrier continued having stool cultures positive for Shigella after treatment with aureomycin and sulfadiazine. A subsequent week of therapy with terramycin, followed by one week's course of aureomycin did not rid the stool of Shigella. The stool finally became negative for the organism after a course of terramycin and polymyxin. The hospital stay was 56 days in this case.

MANAGEMENT

The use of sulfonamides and different antibiotics in treatment of Shigella infections has received a great deal of attention in the past few years. Cheever[1] reviewed the use of antibiotics up to 1952. Garfinkel[4] described experience with the management of 1,400 Korean prisoners. The addition of sulfonamides at first and, more recently, of the broad spectrum antibiotics has been an important adjunct in the management of Shigella enteritis. Lieberman and Jawetz[5] expressed the opinion that polymyxin is particularly useful in the treatment of the carrier state.

It is important in dealing with pediatric cases, however, that, besides the use of specific antibiotic therapy, the broad general principles of management of diarrhea in children and infants be kept in mind. Often children with the disease are severely dehydrated and acidotic. Intravenous administration of a hypotonic balanced electrolyte solution to replace lost fluid and electrolytes in acute cases is an essential aspect of management. Shock, if present, has to be treated by infusion of blood or plasma. For severely toxic, semicomatose children the use of oxygen is an addition to general supportive therapy. Children usually are anorexic during the acute phase of the illness, and only clear fluids are given. As the diarrhea and general well-being improves, a soft low-residue diet can be started to protect the inflamed bowel.

For many years soluble sulfonamides (particularly sulfadiazine) were considered the drugs of choice in the management of Shigella infections. Their usefulness is limited by two factors: (1) the recent observations of increasing numbers of strains of both Shigella sonnei and Shigella Flexner which are resistant to sulfonamides, and (b) the undesirability of giving sulfonamide to a dehydrated child because of the danger of crystalluria and hematuria. Terramycin, aureomycin and chloramphenicol are thought by many observers[2, 4] to be the drugs of choice for Shigella enteritis. The author's experience is too small to warrant any conclusions as to the preference of one antibiotic over another. Neomycin was found to be of very little value in the treatment of acute cases or carriers. Lieberman and Jawetz[5] found carriers to be resistant to any antibiotic therapy. Among the carrier cases in the present study also there was a significant number of failures of treatment with every antibiotic.

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Colostomy Care

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• Psychic preparation of the patient for the necessity of colostomy is a long first step toward his adjustment to living with an artificial anus. Proper surgical placement of the outlet will ease care of the bowel. Control of fecal consistency and peristaltic rate should ideally produce constipation responsive only to habit or enemata. The object of the enema is to produce an evacuation thorough enough to prevent soiling for a day or two. The object of dietary variations is to produce a manageable volume and consistency of fecal stream. The technique of enemas and choice of diet can be individualized when the underlying principles are understood.

OPTIMAL CONTROL of function of the artificial anus and the bowel after colostomy depends upon maintaining proper consistency of the feces and peristaltic rate and upon a desirable constipation responsive to habit or enema.[3] Attention to many minor details—each alone perhaps seemingly unimportant—is necessary for the achievement of these results.

Since the patient's attitude toward colostomy is a great factor, a tactful approach to the matter by way of psychic preparation, before the operation is done, is indicated. Most patients should be told that the proposed operation may entail colostomy. However, the unexpected suggestion of colostomy at the first visit will often stampede a patient. It is usually wiser not to mention the possibility of colostomy until after the patient is hospitalized and has established some confidence in the physician. It is best to discuss colostomy as a procedure that will be used only if absolutely necessary. The patient should be so firmly convinced that, if the operation is done, he will have no lingering doubt as to whether or not it had to be done.

Many laymen have the idea that colostomy is always associated with fatal cancer, or have heard of "messy" palliative colostomy in helpless patients with constantly upset bowels. Without details, the first discussion should create the expectation that the patient will be quite able to live normally and to care for the disposal of feces himself. It is often useful to mention that many people, including senators, singers, actors and athletes are well adjusted to colostomy.

POSITION OF ARTIFICIAL ANUS

An excellent discussion of indications and techniques for colostomy has been presented by Wiley and Sugarbaker.[3] Placement should be preoperatively considered with the patient standing so that the surgeon may observe where on the abdomen a dressing will fit smoothly and be easily accessible to the reach and vision of the patient. Possible loss in weight and unusual occupational activities should be anticipated, as well as the type of clothing or possible desire to wear swimming trunks. A low opening sometimes interferes with sexual intercourse. A periumbilical position might better be avoided if the patient has a deep navel. Incisional herniae, dehiscence and wound infections are dangers in bringing the bowel through the incision. Probably the muscle splitting stab wound in the left lower quadrant is the most common placement.

Submitted September 15, 1954.

SURGICAL TECHNIQUE TO FACILITATE CARE

The hole in the abdominal wall must be just the correct size to make either herniation or stenosis unlikely. Suturing of the bowel wall to the peritoneum, fascia or skin is better avoided owing to the possibility of fistulae from the stitches. At the completion of the operation the stoma should be left an inch and a half above the level of the skin so that after postoperative contraction it will be just about a half-inch above the skin level. If the subcutaneous fat is excessively thick, the skin about the stoma can be "umbilicated" by tacking the skin to the underlying fascia with a few interrupted sutures. A stump that looks perfect at the operating table will probably shrink and be too small later, whereas an error on the generous side can be corrected later by trimming in the office. It is easier to free the bowel to provide adequate exteriorization at the time of operation than it is to correct retraction of the stoma.

For the surgical dressing, vaseline gauze wrapped around the external stump of bowel should be placed in such a way that only the top layers need be disturbed to create the vent when the stoma is opened. Even though apparently soiled, these sealed underlayers of vaseline gauze upon the serosa and skin edges can remain adherent for several days. This

wrapping of gauze serves to maintain the bowel in position while it seals and heals to the abdominal wall. A similar function is served by the clamp, on an end colostomy, which is left incorporated in the dressings.

POSTOPERATIVE CARE

In cases of obstruction of the bowel, a catheter may be placed immediately after operation to permit decompression. Usually, however, the opening is not made until 48 hours later. By then, in most cases, sealing of the peritoneum and of the edges of the wound has taken place. An even greater length of time may elapse if there is no indication of the development of obstruction. The external portion of bowel should be glanced at daily to note its color and to make sure it has not slipped back inside. With loop colostomy, the presenting antimesenteric border of the bowel may be opened with cautery to seal bleeding points. Occasionally ligation of a bleeding vessel is necessary. With proper preoperative preparation of the bowel, there is usually no need for irrigating after colostomy before the fifth or sixth day. However, if preparation was inadequate or the bowel was obstructed at the time of operation, irrigation a day after the opening may be desirable. The first irrigation is best performed by a physician or a thoroughly experienced nurse. With the patient lying on the left side, a large well-lubricated catheter is inserted gently to a depth of six inches or so. It cannot be forced, for danger of perforation definitely exists. If the catheter will not pass a fold of mucosa, water run through it will usually open the way ahead. Some sort of cuff (such as an inverted rubber nursing nipple) around the catheter may be necessary to prevent reflux spilling of the water. In the first few days it is not essential to continue enemas until all the contents of the bowel are evacuated.

Some surgeons administer a cathartic on the third to fifth postoperative day when the patient is accepting feedings. This liquefies the feces and overcomes inertia of the bowel induced by narcotics and ileus.

THE COLOSTOMY ENEMA

As soon as possible the patient should be taught to care for his own bowel, the nurse doing no more than handle the equipment and supervise. The enema should be given at the same time each day in order to establish a habit, the time of day chosen being one that will be convenient for the patient after returning home. Usually no more than a pint of fluid administered once or twice is necessary. Although the first irrigations are given with the patient in bed, it is soon more satisfactory for him to use commercial irrigating equipment while sitting on a chair before the open toilet. After the patient has cared for himself for a few days, he then should carry out the procedure while the physician watches to point out errors or demonstrate improvements and modifications in technique.

The object of the enema is to produce a reflex evacuation of the entire colon, ideally even of the cecum. It is not necessarily intended to wash out the entire cecum. The evacuated bowel will then store without emptying for another 24 to 48 hours. However, in some cases the bowel will not be satisfactorily emptied for long enough with a simple stimulating irrigation. Adequate cecal cleansing may require a high enema through an inflated Foley catheter which is collapsed and withdrawn after the cecum has been filled with water. At first it takes about an hour to give an enema through the artificial anus and completely evacuate the bowel, but later the patient learns to wear a bag after the enema to collect the discharge in less than an hour. After evacuation, the patient should feel secure with only a small dressing or Kleenex beneath an elastic girdle. If protracted delay between administration and return of the enema occurs, a little soapsuds may be added to the water. Cramps may result if the water is injected too rapidly or is too cool.

With an artificial anus, constipation is desirable so that evacuation occurs only by some habit-reflex or with an enema. Some patients develop such spontaneous regularity that irrigations are not needed. Many need the enema daily whereas others can go as long as two or three days between enemas without soiling. It is best to commence with daily irrigations and gradually increase the interval as the bowels become regulated and the contents solid. In rare patients with an irritable bowel, soiling several times daily may persist despite all efforts. In these cases a daily high enema should be continued and a dome or bag worn in the interval. The only exception to the rule against laxatives is the case of the rare person in whom the bowel contents become so firm that, despite enemata and liquids by mouth, the feces still are inspissated.

DIET

Manageable consistency and volume of fecal stream is the objective of diet. Most patients are finally able to return to their customary diet. A few always have to avoid any but constipating foods and milk, refined cereals, cheese, fish, beef, bread, potatoes, macaroni, rice and foods that have little indigestible residue. Such foods as fresh fruits and juices, green vegetables, whole cereals and breads, cabbage, beans and corn produce considerable residue or are laxative and should be avoided until the patient learns by adding one at a time what can be tolerated. Certain fruits and juices may increase peristalsis and should be used only when the stools

get too hard. Prohibited foods (which usually interfere with regularity) include spices, uncooked or fibrous vegetables, iced or carbonated beverages, all fried foods and usually pork, veal and duck.

Peristaltic activity and the time taken for foods to pass through the gastrointestinal tract depend much upon diet. Diminution of peristalsis can be accomplished when necessary with cholinergic drugs such as amphetamine sulfate administered postprandially so as not to interfere with the appetite.

CARE OF STOMA AND SURROUNDING SKIN

During the first postoperative weeks, the exposed serosa and mucosa may be very friable and bleed upon removal of dressings. Hence fine-mesh vaseline impregnated gauze is preferred. If cellulitis develops around the stoma, it is treated with warm, moist compresses and antibiotics, and the removal of any stitches restricting drainage.

Unless there is diarrhea there is usually no irritation of the skin about the artificial anus formed by colostomy. Should cutaneous irritation develop, cleanliness, exposure to air and the use of an ointment containing thymol iodide or a silicone is ordinarily effective. Inability to control flatus may be made less embarrassing by consumption of charcoal tablets or chlorophyl. Herniation of the stoma or of the area about it, if bothersome, can be reduced and held inverted by a bulky pad worn beneath a corset or supporter. If manipulation is necessary to keep the stoma adequately dilated, the patient or a relative can be taught to insert an index finger into the opening once or twice a week. If strictures occur they are almost always at the mucocutaneous junction, and surgical correction is necessary. Usually the operation is relatively minor and it should not be postponed so long that the opening becomes so small that more extensive revision is demanded.

INFORMATION TO PATIENT

Minimum instructions to the patient should include the information listed below. (They should be provided in writing if the patient has difficulty in remembering or understanding them.)

1. Irrigate with a quart of lukewarm tap water at least once a day at a regular time. The container should be elevated about a foot above the level of the opening in the abdomen. A lubricated catheter should be inserted slowly and gently six to eight inches and the water allowed to run in slowly. When all the water has run in, the catheter should be removed and at least 30 minutes allowed for the returns to be expelled.

2. After the enema has evacuated, do not wear a colostomy bag. Cover the abdominal opening with Kleenex held in place by a wide elastic abdominal band or girdle.

3. Keep the colostomy opening wide by inserting the index finger past the second joint about twice a week. (Rubber finger cots can be purchased at the drug store for this purpose.)

4. Take no laxatives. Avoid fruits which produce bowel irritations or looseness, such as certain raw fruits, beans, corn and spices. If the feces are too hard, drink more water.

5. Remember that ideally the bowel should remain constipated and evacuation should occur only when it is expected to or when irrigation is carried out.

446 Piedmont, Glendale 6.

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Planned Care for Patients with Bronchiectasis

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• *Bronchiectasis, for which once only the most elementary palliation could be offered, now often can be cured by operation or well controlled by conservative therapy.*

Since true bronchiectasis implies irreversible anatomic changes, operation offers the only hope of cure, and it should be undertaken whenever it is not contraindicated by extent of involvement, age of the patient or other factors. Surgical results are excellent and mortality is at a minimum.

When operation is prohibited, good results can still be anticipated by conservative measures. Such conservative therapy should combine prolonged use of antimicrobial drugs with adequate drainage of the diseased segments and general supportive measures. Any residual infection can be controlled by moderate use of appropriate antimicrobial agents.

It is emphasized, however, that the control of bronchiectasis requires very careful diagnostic studies and a detailed analysis of the patient's condition, and that the therapy itself must be carefully adjusted in terms of the individual situation.

TWENTY-FIVE YEARS AGO bronchiectasis was regarded as a chronic disease largely beyond the reach of medical care. The patient could be palliated by postural drainage and by the general hygienic regimens used in tuberculosis, and the bad breath and fetid sputum characteristic of the disease could be ameliorated by creosote. But with or without medical treatment the patient could usually be expected to die within ten years after diagnosis. In a few instances, advanced cases of bronchiectasis were approached surgically by such desperate procedures as thoracoplasty and cautery pneumonectomy, with occasional improvement as a result.

This generally hopeless prognosis of a few short years ago has of course been almost completely reversed. At present, complete cure is often possible by means of surgical extirpation, and in almost every other case the disease can be controlled indefinitely by modern medical therapeutic techniques. This is not to say that the management of bronchiectasis is simple. Underlying the infectious process of true bronchiectasis are irreversible pathological changes in lung structure; and these changes complicate therapy. Each case is an individual problem, and the medical approach to it must be planned in detail if treatment is to be successful. To borrow a military metaphor, bronchiectasis cannot be controlled by a single battle, but only by a carefully planned and conscientiously followed campaign.

DIAGNOSTIC CONSIDERATIONS

The clinical symptoms of bronchiectasis have been accurately described for many years, but since they are the same as those of any other chronic bronchopulmonary suppuration, it is necessary to accurately establish the diagnosis of bronchiectasis and to delineate the extent of the disease. Unless the lesions are so grossly visible on ordinary x-ray films of the chest as to make it superfluous, bronchography is an indispensable procedure. Ideally, both lungs should be entirely mapped with iodized oil even though several roentgenographic studies are required. This is essential for the evaluation of the patient for surgical treatment and is valuable in planning adequate postural drainage. Contraindications to such studies include sensitivity to iodized oil or to local anesthetics.

In a significant number of cases bronchiectasis is secondary to demonstrable bronchial obstruction or stenosis. X-ray films can suggest this possibility, but they are not a substitute for direct bronchoscopic visualization of the bronchial tree. Tumors, foreign bodies or bronchial stenosis secondary to inflammatory changes may be recognized and appropriately treated. Bronchoscopic examination should always be considered in the evaluation of a case of bronchiectasis. In addition to its direct aid to diagnosis this procedure can be very helpful in clearing major bronchi of inspissated mucous plugs and other debris. Cytologic studies for malignant cells should be done routinely.

GENERAL MEASURES

When a diagnosis of bronchiectasis has been made, treatment should begin with hospitalization if this is at all possible. In part, hospitalization is

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desirable in order to facilitate the control of all the secondary factors which may contribute to the primary disease process. Proper rest, adequate nutrition and hygienic conditions can thus be assured. Anemia, if present, (as it often is with bronchiectasis), can be treated intensively. Also, psychological depression which frequently accompanies bronchiectasis can be dispelled.

Furthermore, hospitalization permits the full investigation and treatment of associated diseases. Chronic upper respiratory tract infections, particularly sinusitis, which continually "feed" the damaged lung segments, must be controlled before control of bronchiectasis is possible. Allergic reactions that bring about bronchospasm and mucosal edema, and thus interfere with drainage, must be controlled. Underlying nutritional disturbances such as occur in mucoviscidosis (pancreatic fibrosis) must be diagnosed and treated appropriately.

SURGICAL TREATMENT

Bronchiectasis is perhaps unique among infectious diseases in the fact that surgical operation, if possible, is the procedure of choice. It offers the only hope of real cure, and, further, this cure can be effected without serious postoperative disability if reasonable care is used in the selection of patients. The great advantages of operation have become particularly apparent since segmental resection was introduced by Churchill and Belsey in 1939.

Each surgeon will of course apply his own criteria of operability. In general, it can be said that the most critical factor is the amount of tissue involved. Although the hazard of a major operative procedure naturally increases with the age of the patient, operation is not necessarily precluded by an age of 50 or even 60 years. Neither is it precluded by bilateral disease, if the total area involved is not too great. The most important contraindications are (1) irreversible bronchospastic states resulting from allergic reaction or chronic infection or (2) fibrosis and emphysema, which are in themselves disabling.

To no small degree, the desirability of surgical treatment of bronchiectasis is due to the remarkable achievements that have been made in this field of thoracic surgery in the past 15 years. At present, hospital mortality ordinarily does not exceed three per cent, even when cases of bilateral disease are included in the computation. In addition, about 75 per cent of the patients who are operated upon are completely cured and another 15 per cent have only mild residual symptoms. Only about 10 per cent of the operations are classified as failures.[4, 6]

There is little doubt that even this impressive record can be improved upon by rigorous preoperative studies. A large portion of the failures heretofore recorded have been classified as due to "incomplete operation." This can be avoided in almost every instance if both lungs are completely mapped with iodized oil. It should be recognized that bronchograms are not without their limitations. Failures of the kind attributed to a preexisting bronchospastic state or to irreversible fibrosis and emphysema can also be minimized by thorough diagnostic studies, although admittedly these conditions are more difficult to evaluate. Surgical complications, another cause of failure, are of course already incalculably reduced by intensive preoperative medical therapy, as well as by continued improvement in surgical technique and anesthesia. The development of new areas of bronchiectasis in the distorted residual segments is a fourth possible cause of failure.

A case report illustrates the typical surgical situation:

A 32-year-old white housewife who was first observed in January of 1945 said that she had had recurrent chest colds since 1941 and in the summer of 1943 had had "virus pneumonia." Since that time she had raised a teaspoonful of "vile-tasting" yellow sputum a day; and there had been several episodes of hemoptysis shortly after recovery from pneumonia. The patient complained of chronic fatigue.

Upon examination the right middle lobe appeared to be the source of the sputum, and postural drainage and treatment with penicillin were instituted, with some relief of symptoms. Pregnancy delayed further evaluation, but the patient returned in October of 1945. At that time bronchography revealed cylindrical bronchiectasis in the right middle lobe (Figure 1). The patient refused to undertake intensive therapy of any sort at that time, but about a year later she finally consented to resection, and the right middle lobe was removed. Thereafter there were no complaints referable to the chest, except for an occasional cold.

It does no disservice to medical terminology to label the foregoing case a cure. Although this kind of operation is still too new to permit certainty in the matter, there is no physiological reason apparent for supposing that this patient is not essentially "normal," with the general life expectancy of her age group.

CONSERVATIVE TREATMENT

It must be reiterated that only operation offers hope of cure in bronchiectasis; the anatomic and physiologic abnormalities characteristic of the disease are not amenable to conservative therapy. On the other hand, a well-balanced and judicious program of conservative therapy can control the disease in almost every instance, and it can restore the patient to normal life within reasonable limits. However, this possibility can only be realized by intensive and prolonged treatment.

The first step in conservative therapy is to effect maximum drainage of the infected area. In many

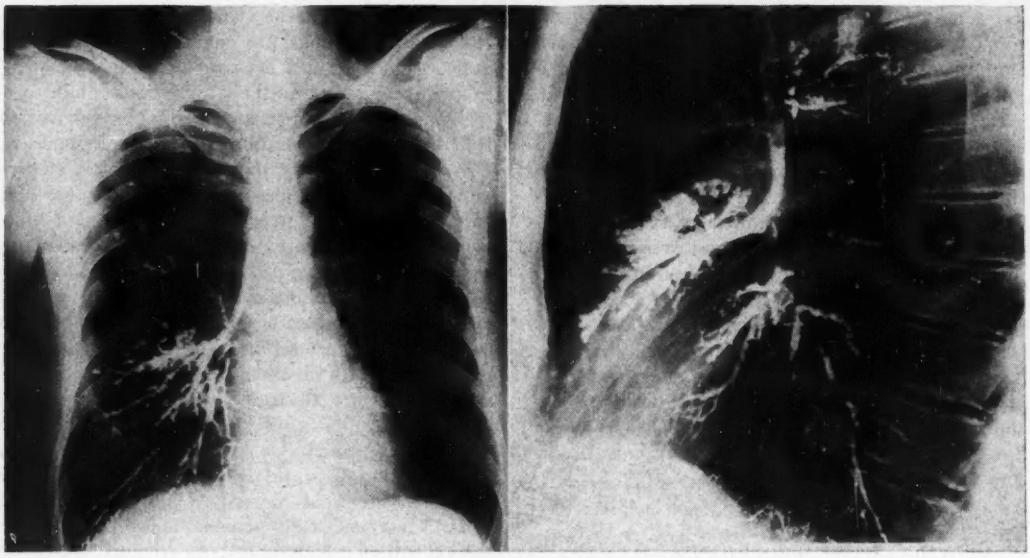

Figure 1.—Cylindrical bronchiectasis in the right middle lobe.

instances the contribution that bronchoscopy can make to this end is very important, since it permits aspiration of the inspissated mucous plugs and other debris difficult to approach in any other way. Local bronchoscopic instillation of antibacterial agents may be accomplished at the same time. Postural drainage, however, remains the most important technique available for the removal of bronchial secretions. It should be done routinely several times a day and should be continued even after the infection has begun to respond to antibacterial therapy. The facilitation of expectoration by various pharmacologic preparations has long been practiced, but the availability of mucolytic enzymes[7] and detergents has added a whole new dimension to this kind of therapy. The enzymes, highly purified trypsin (Tryptar®) and Streptokinase-Streptodornase,® must be used with caution.[3] At times they produce a frothy sputum so thin that it is difficult to expectorate; they may also induce a considerable degree of bronchospasm. A detergent, Alevaire® (Triton WR 1339, 0.125 per cent in combination with 2 per cent sodium bicarbonate and 5 per cent glycerin) has been found to assist liquefaction of sputum in many cases without harmful side-effects. This substance has the additional advantage of being chemically inert, so that it may be used as a vehicle for antibiotics, bronchodilators and vasoconstrictors. It may be administered by a nebulizing technique.

In many, if not in most, cases of bronchiectasis there is some degree of bronchospasm as well as mucosal edema, both of which impede the drainage of secretions. Phenylephrine (Neo-synephrine®) is a decongestant of value. Bronchospasm generally responds well to either racemic epinephrine solution (Vaponefrin®) or to isopropylarterenol hydrochloride (Isuprel®). In the authors' experience these drugs have been most effective when administered by means of a Vaponefrin nebulizer connected to an oxygen tank through a "Y" tube, or in a Bennett Intermittent Positive Pressure Therapy Unit. They should be administered just before postural drainage. If the effect of these bronchodilators is unsatisfactory or they are not tolerated, aminophylline may be found to be of value in the condition.

In most cases, a combination of the above-described techniques is sufficient to assure the first objective of therapy, an adequately drained bronchial tree. When it is obvious that these measures do not permit drainage, the problem is generally tussic insufficiency, owing to deficient aeration in the bronchiectatic segments. This condition is most likely to occur in chronic cases of long standing. Therapy must be directed to the increased ventilation of such segments. Perhaps the two devices designed by Barach, the exsufflator and the artificial cough chamber, accomplish this most effectively; but both devices require modified respirators or lung-immobilizing chambers, which are not yet generally available.[1, 2] The authors have obtained excellent results with the Bennett Unit, which provides intermittent positive inspiratory pressure with a rapid fall to atmospheric levels upon expiration. The Bennett Unit not only helps in the ventilation of diseased lung segments, it permits the simultaneous nebulization of bronchodilators, antibiotics and other drugs.[5]

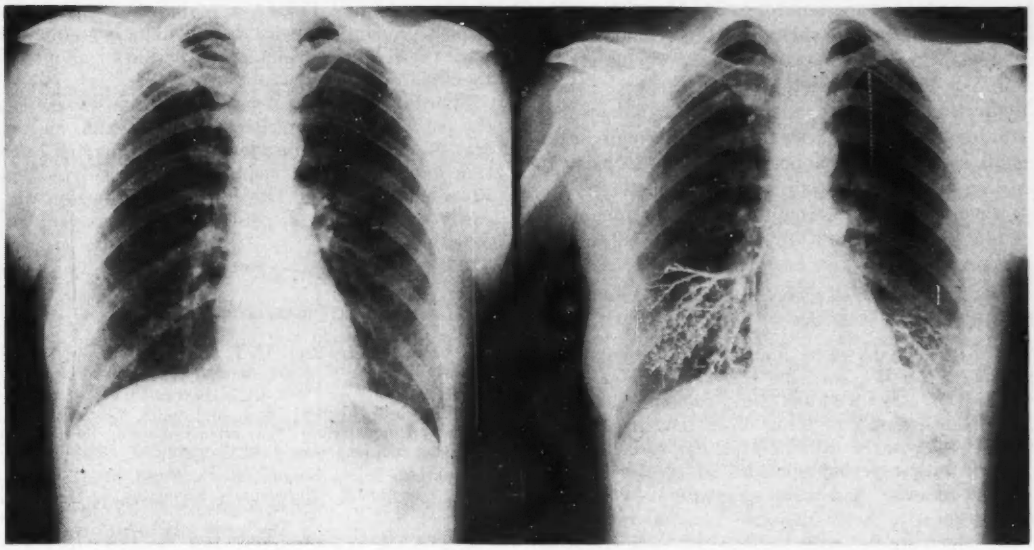

Figure 2.—Roentgenograms with contrast medium, showing extensive bronchiectasis in left lower lobe.

The basis for modern conservative treatment of bronchiectasis is intensive and prolonged use of antimicrobial agents. Success depends in great measure upon two principles—careful selection of drugs, and persistence in maintaining therapeutic levels of the selected drugs. Because of warning as to toxicity and the dangers of resistance and sensitization, there has been a good deal of reluctance to use these drugs over prolonged periods. The authors' experience, however, has indicated that over-extended use is preferable to incomplete therapy. Sensitization and the development of resistant strains has not been particularly troublesome and side-effects have been minimal; and it is believed that resistant organisms are usually the product of incomplete and haphazard treatment rather than of undue prolongation of therapy.

Before therapy is started, sensitivity studies should be done upon the organisms cultured from the sputum, because of the ever-increasing incidence of resistant organisms. Penicillin and streptomycin are usually the drugs of choice if they are effective against the organisms in the sputum, for they do not predispose to monilial infection. Penicillin and streptomycin are usually continued for one to three months. Erythromycin may also prove to be valuable because of its antibacterial range. In smaller doses it may be maintained for up to a year. In general, it is very important that antibiotics be prescribed that will be effective against the entire range of microorganisms present in the sputum. Repeated cultures should be made during the course of therapy to detect the appearance of resistant strains or of organisms not affected by the antibiotics used as indicated by the clinical course.

It should be pointed out that the content of antibiotics in the sputum is at least as important as the content in the blood. Since the flow of blood through bronchiectatic lung segments is often greatly impaired, blood levels that otherwise would be adequate cannot be assumed to guarantee effective therapy. For this reason, the inhalation of nebulized mists of antibiotics, or of micronized dusts, can contribute considerably to therapy. The sulfonamides and penicillin, streptomycin and terramycin have been most commonly used in these ways.

Intensive antimicrobial therapy should be continued for at least two weeks after all grossly purulent elements have disappeared from the sputum. Then dosage should be gradually reduced, and, if no recrudescence occurs, intensive therapy should be discontinued. Further antimicrobial therapy with preparations such as sulfonamides or erythromycin for oral administration should be administered for a period of many months, until it becomes clear that all residual infection has been eliminated. This is, of course, ambulatory therapy, during which the patient may pursue normal activities.

Bronchiectatic patients remain especially liable to acute respiratory infections, but these may be easily controlled by brief courses of intensive therapy. Otherwise they should be restored to full activity within the limits set by the amount of functioning lung tissue remaining.

At times bronchiectasis of long standing will not clear completely under this procedure. Excellent success in controlling such cases, however, has been obtained by continuing medication in reduced dosage on a semi-permanent basis. The sulfonamides are excellent for this purpose, since they can be

taken orally and the development of resistance has not been a serious problem. By this means the patient may be kept free of bronchial symptoms indefinitely and restored to excellent general health. Medication in some patients can be temporarily withdrawn during the summer months and begun again each fall. Chemoprophylaxis has a place in dealing with bronchiectasis comparable to its use in rheumatic fever. Small doses of sulfonamides (1 to 2 grams per day) are useful in preventing new infection with sensitive bacteria.

The following case report illustrates the conservative therapeutic procedures:

A 51-year-old white housewife, first observed October 31, 1949, said she had raised thick green sputum for as long as she could remember, usually upon bending over or lying down. During the previous winter three attacks of hemoptysis had occurred, with repeated episodes of pleurisy. Nasal allergic disease had been controlled by dietary limitation.

Roentgen studies with Lipiodol showed extensive bronchiectasis in the left lower lobe (Figure 2). Conservative therapy was insisted upon by the patient and she was admitted to the hospital in November. Besides postural drainage, a course of combined penicillin and streptomycin therapy was instituted, both intramuscularly and by nebulizer. At the end of two months, sputum had become mucoid and there was pronounced improvement in subjective symptoms. The patient was discharged from the hospital and put on a regimen of 1.5 gm. of triple sulfonamides twice daily. This was maintained until the following summer—a period of about five months.

When last observed more than four years later the patient was in excellent general health, and except for occasional episodes of acute bronchial infection once or twice a year she had been free from bronchial symptoms. The episodes of infection were easily controlled with penicillin, erythromycin and other antibiotics.

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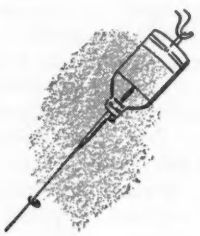

Diuretics in Therapy of Epilepsy

Their Use for the Potentiation of Anticonvulsant Drugs

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• *Animal experiments having indicated a nearly twofold increase in anticonvulsant protection with the use of diuretics which increase blood-brain barrier permeability, the principle was applied to treatment of humans with epilepsy. The addition of diuretics to anticonvulsant medication permitted a decrease of previously toxic dosages in ten epileptics, followed for six months, without lessening (and in some cases improving) the control of seizures.*

In three cases excessive diuresis and gastric distress necessitated discontinuance or decrease in dosage of the diuretic used.

IT IS GENERALLY AGREED that regardless of the method followed or medication used, approximately 25 per cent of epileptic persons cannot be rendered entirely free of seizures. As the number of commercially available anticonvulsants reaches the dozen mark, it also becomes increasingly obvious that most of the drugs introduced during the past decade pose serious problems owing to their toxic effects. When the functions of the liver and hematopoietic system become involved, besides mere intolerance, danger to life has to be seriously considered. The 25 per cent of epileptic persons who cannot be entirely freed of seizures are at present being treated on the basis of an unsatisfactory compromise between efficiency and toxicity. Adequate amounts, therefore, are often not tolerated.

It is assumed that drugs are selected for anticonvulsant trial on the basis of (a) the presence of certain radicals in the formula; (b) their ability to provide protection against experimentally produced convulsions; (c) their low toxicity. If experiments indicate that a preparation is high on the list from the point of view of anticonvulsant protection, yet low with regard to deleterious effects, it is then ready for a tryout on humans with epilepsy. It is further assumed that while the point of action of such a drug is in the brain, not all of the dose reaches its destination. One filter point exercising control over the drug absorption is the blood-brain barrier. The critical anatomical substratum of this barrier is believed to be the endothelial lining of the cerebral capillary bed.

For a working hypothesis it is assumed that any mechanism that could increase the permeability of the blood-brain barrier is likely to increase the drug's absorption by and passage into the brain. While the exact site of action of anticonvulsants is still not well known, certain it is that they should exert their maximal action at the point of origin of the electrical storms which, through a series of facilitatory processes, detonate a wide number of neurons into a clinical epileptic attack. Probably the most intensive increase in blood-brain barrier permeability is brought about (in experiments on animals) by exposing the head to the effect of ultrasonic treatment. This method is not entirely safe apart from the fact of its being impractical for possible routine use in humans. It proved to be preferable to use the large reservoir of diuretic substances which are known to increase general tissue permeability including that of the blood-brain barrier. Instead of chemical analysis of the blood on one hand and the cerebrospinal fluid on the other, the passage of the drugs under study was monitored with the aid of electroencephalograms, upon which both convulsants and anticonvulsants print a typical, clearly identifiable pattern that could serve as an end point.

The original impetus for such a utilization of diuretics was supplied by Frölich and Zak,[5] who succeeded in producing clinically satisfactory strychnine and morphine effects in frogs with lower than average doses if they previously treated their animals with the diuretic, theophyllin. Blood-brain barrier permeability in connection with epilepsy (and other neurological diseases) has been under scrutiny from another direction by Cobb[4] and particularly by Aird.[1] On the assumption that seizures might possibly occur either during increased permeability to metabolic noxi or undue ingress into the brain of normal blood constituents, they attempted to raise the barrier by the use of vital dyes

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which, according to Spatz,[7] have the singular property of settling down in the endothelial lining of the capillaries. While this treatment was pursued with initially encouraging results, it should also be pointed out that Katzenelbogen,[6] using the bromide infiltration method, was not able to prove statistically a direct relationship between increased seizure liability and high blood-brain barrier permeability.

The starting point of the experimental part of the work here reported upon was a paper by Ziskind and Bercel[8, 9, 10] which indicated that slow intravenous injection of 1 per cent Metrazol® solution in rabbits produces a preconvulsive seizure discharge which can be delayed by prior treatment with anticonvulsants. The delay in the appearance of the end point, expressed in milligrams of Metrazol, was considered a measure of anticonvulsant protection. The minimum electroencephalogram distortion dose for anticonvulsants was established by the earliest appearance of sleep patterns in the electroencephalograms of animals that received increasing amounts of anticonvulsants.[3]

Forty rabbits were used to test the anticonvulsant-enhancing effects of diuretics.[2] It was found that the first seizure discharge occurs after injection of 9 mg. of Metrazol. When the animal was protected by 40 mg. of phenobarbital given by vein (double the minimum distortion dose) for three minutes, the seizure discharge occurred after 22 mg. of Metrazol. When the animal was prepared with theophyllin sodium acetate, 15 mg. per kilogram of body weight, and after three minutes the 40 mg. per kilogram of phenobarbital was administered followed in another three minutes by Metrazol, the first seizure discharges occurred after 15 mg. However, when the same experiment was repeated with the difference that ten minutes elapsed between theophyllin and phenobarbital administration, the seizure discharge did not occur until after 42 mg. of Metrazol was introduced intravenously. All these figures were average values.

The time elapsed between the administration of theophyllin and the administration of phenobarbital, therefore, appeared to be critical. It seems that when phenobarbital is given as early as three minutes after the diuretic (when the concentration of diuretic is still high) anticonvulsant protection is actually reduced from 22 mg. to 15 mg. It is believed that the initial cerebral stimulant effect of theophyllin is responsible for this phenomenon, it being known that very large doses of this diuretic can even produce convulsions. Large concentration of theophyllin, therefore, acts synergistically with Metrazol. When the time interval is at least ten minutes, the gradual dilution of theophyllin cuts down its stimulant effect while the permeability-raising action becomes prevalent. Thus, the anticonvulsant protection is enhanced nearly twofold from 22 mg. to 42 mg. of Metrazol.

Another set of experiments indicated that theophyllin, followed in ten minutes by phenobarbital, lowered the minimum distortion dose from 20 mg. to 10 mg. This means that spindles indicating sleep in the electroencephalogram appeared with half the dose if the animal's blood-brain barrier permeability has been raised by the diuretics. Salyrgan® 1 per cent, 5 mg. per kilogram of body weight, and theobromine sodium salicylate 1 per cent, 20 mg.

RESULTS OF ADDING DIURETICS

Case	Type	No. of Seizures per Month —Before and After Addition of Diuretic— Before	After	Toxic Effects of Anticonvulsants —Before and After Addition of Diuretic— Before	After	Anticonvulsant Therapy (Doses* per Day) Phenobarbital Before	After	Dilantin® Before	After	Mesantoin® Before	After
1	Grand Mal	2	0	None	.....	1	1	4	4		
	Petit Mal	120	10								
2	Grand Mal	0	0	Rash	Eliminated			7	4		
	Petit Mal	6	6								
3	Jacksonian	8	0	Nausea and vomiting	Eliminated	2	1	5	5		
4	Grand Mal	0	0	None	.....			2	2		
	Petit Mal	60	60								
5	Grand Mal	0	0	Leukopenia	Eliminated	1	1				
	Petit Mal	12	0								
6	Grand Mal	2	1	Constipation	Eliminated	2	1	7	6		
	Psychomotor	4	4								
7	Grand Mal	1	½	Leukopenia	Eliminated	2	2			6	3
	Petit Mal	0	0								
8	Grand Mal	2	1	None	.....	1	1	5	5		
	Jacksonian	12	8								
9	Petit Mal	6	0	None		1	1				
10	Petit Mal	160	160	Leukopenia	Eliminated			2	2		

*Single doses for various drugs follow: Phenobarbital, 0.1 gm.; Dilantin, 0.1 gm.; Mesantoin, 0.1 gm.; Tridione, 0.3 gm.; Mysoline, 250 mg.

per kilogram, had the same effect as theophyllin. Tridione® could be substituted for phenobarbital. These studies suggested that diuretics facilitated the admittance of anticonvulsants in the brain in doses that ordinarily did not alter the electroencephalogram.

In order to test this principle in humans with epilepsy, ten patients of the kind previously mentioned—in whom adequate anticonvulsant medication had toxic effect—were carefully selected. The patients ordinarily had seizures with sufficient frequency to permit relatively rapid evaluation of the therapeutic effect. The medication they were receiving at the onset of this trial represented the optimum regimen achieved after long experimentation with a combination of drugs. The monthly number of seizures was determined for a six-month period before the addition of the diuretic to the anticonvulsant medication they were receiving. This was then compared with the monthly seizure averages of another six-month period following the addition of diuretics to the drugs usually taken. Where the amount of anticonvulsant had to be reduced because of toxic side-effects, the reduction was done slowly during the first of the six-month periods. The results are shown in Table 1. The following case history serves as an example of the successful use of the diuretic:

REPORT OF A CASE

The patient was a 16-year-old girl who had had idiopathic epilepsy (predominantly petit mal, rarely grand mal) since the age of nine years. After extensive clinical trial, she was given 1.5 gm. of Tridione daily in divided doses and 90.0 mg. of phenobarbital. The major attacks were eliminated but the patient still had an average of 12 petit mal seizures a day. When the amount of Tridione was increased to 2.3 gm. daily, as was done on several occasions, seizures stopped but leukopenia developed—2,000 leukocytes per cu. mm. on one occasion. Theominal (theobromine, 0.3 gm., and phenobarital 30.0 mg.) thrice daily was added to the regimen and thereafter the patient was free of seizures with the dosage of Tridione at 0.9 gm. daily.

The diuretic most often used was theobromine, 0.3 gm., with or without phenobarbital and theophyllin, .09 gm. to 0.15, twice or thrice daily. These tablets were taken with meals and the anticonvulsants were given after eating. In only one case was diuresis so increased that the diuretic had to be omitted; and in two cases theophyllin caused nausea, necessitating a reduction in dosage.

Toxic symptoms such as leukopenia, exanthema, gastric distress, constipation, headaches, nausea, vomiting and lymphadenopathy, which appeared with large amounts of medication, disappeared with the reduction in dosage; and after the reduction the lesser amount was either more effective clinically or as effective as the same amounts had been before. No patient had more attacks than before.

The economy in medication amounted to an average of 30 per cent (range 10 to 50 per cent). A more important advantage, however, was the patients' ability to tolerate some of the drugs for the first time.

It is not yet certain that the diuretics used and the dosages in which they were given are the best available. Experiments with a number of substances

0 ANTICONVULSANT THERAPY

Before and After Addition of Diuretic						Type of Diuretic and Number of Daily Doses		Summary of Effects of Addition of Diuretic		
Tridione®		Mysoline®		Milontin®						
Before	After	Before	After	Before	After	Diuretic	No.	Seizures	Dosage of Anticonvulsants	Toxic Effects
				6	6	Theominal	3	Reduced	Same	*None before*
						Theophyllin	2	Same	Reduced	Eliminated
						Theominal	3	Reduced	Reduced (Sedative only)	Eliminated
		5	1			Theophyllin	2	Same	Reduced	*None before*
5	3					Theominal	3	Reduced	Reduced	Eliminated
						Theobromine	3	Reduced	Reduced	Eliminated
5	5					Theobromine	3	Reduced	Reduced	Eliminated
						Theominal	3	Reduced	Same	*None before*
				9	6	Theominal	3	Reduced	Reduced	*None before*
6	3	4	1			Theophyllin	2	Same	Reduced	Eliminated

Milontin, 0.3 gm. Diuretics: Theominal = Theobromine, 0.3 gm. + phenobarbital 30.0 mg.; Theophyllin, 0.09 — 0.15 gm.; Theobromine, 0.3 gm.

combined in one capsule with the various anticonvulsants are being carried on. The results appear to be sufficiently encouraging to warrant further more extensive clinical trial.

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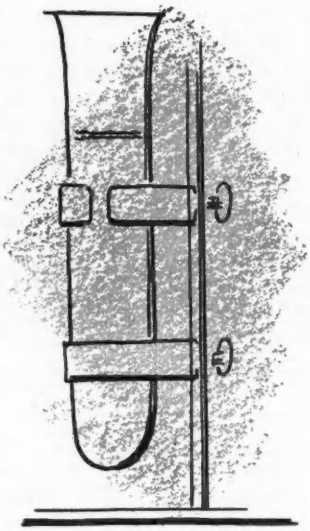

A Laryngologist Looks at Cigarettes

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• The relationship between cancer of the lung and cigarette consumption is far from proved. It would appear from observations and experiments cited that some form of filtration of smoke is better than none. It is important that physicians be sufficiently acquainted with the subject to enable them to advise their patients concerning cigarettes and cigarette smoking.

WHAT IS THE TRUTH about cigarettes? Are they really irritating; do they cause cancer? What brand or type of cigarette would you recommend? These are some of the questions being asked of physicians today.

Most of the present-day impressions concerning the effects of cigarette-smoking upon the structures of the respiratory tract have not come from the medical profession; unfortunately they have originated with the advertising agencies who have issued much misinformation on the subject.

The influence of excessive smoking upon the cardiovascular system is well known. It is only recently, however, that the effects of smoking upon the respiratory tract have been given much attention. In the author's opinion, one who smokes more than 20 cigarettes a day is smoking excessively, although half that many may be too much for some persons.

The relationship of excessive smoking to cancer of the lung is regarded by some investigators as established. Despite the excellent articles of Wynder and Graham,[16] Doll and Hill,[4] Ochsner and DeBakey,[11] Mills and Porter,[9] and Lindskog and Bloomer[8] which indicate a steady increase in the incidence of cancer of the lung, mostly in smokers, there are many considerations which are not in full agreement with the suggestion of such a relationship.

Some of the facts which must be taken into consideration follow. Cancer of the lung occurs in nonsmokers. The rise in the occurrence of lung cancer came at the turn of the century, whereas the first pronounced increase in cigarette consumption occurred immediately after the first World War. It is significant that the diagnosis of cancer of the lung has been more accurate and more readily made in recent years because of better facilities and greater cooperation from the average patient. The reported incidence of cancer of the lung is highest in areas where hospital and diagnostic facilities are better; in Idaho where the annual per capita consumption of cigarettes is 2,003 the incidence of this condition in relation to cancer at all sites is 2.9 per cent, while in New York State with an annual per capita consumption of 2,319 cigarettes the incidence is 11.9 per cent. Also the reported incidence of cancer of the lung is higher in urban than in rural areas. In 1936, Arkin and Wagner estimated that 20 years before, primary lung cancer was diagnosed in only 5 per cent of cases; by 1936, the figure had risen to 50 per cent. More persons now survive severe infections than ever before and live on, later to die of cancer of the lung and other conditions. A Foreign Letter published in the *Journal of the American Medical Association*, May 1, 1954, stated that in 1952 in England and Wales 11,981 males and 2,238 females died of cancer of the lung. The figures also showed that the highest mortality rate for this disease was in the age group 65 to 74 years for males and 75 years and over for females.

Although evidence of excessive cigarette smoking frequently is seen in the pharynx and larynx, the rise in incidence of cancer of these structures has not kept pace with that of lung cancer. It has been shown that the carcinogenic factor in cigarette smoke is relatively mild (Bogen[3]). Certain tars isolated from cigarette smoke have produced skin cancer in mice. This, however, is not considered conclusive evidence that cigarette smoke contains a substance capable of producing cancer of the lung in man. These are some of the considerations which suggest that by no means are all cases of cancer of the lung due to cigarette smoking. Can it be that the relationship between cancer of the lung and cigarette smoking is coincidental?

Otolaryngologists should be acquainted with the effects of smoking and should have some knowledge of the various brands of cigarettes and filters.

While much has been printed and broadcast concerning the effects of cigarette smoking on the nose and sinuses, it is important to recognize that these structures are rarely significantly affected by this act. Only if a smoker deliberately and habitually exhales through the nose would the nose and sinuses show evidence of congestion. Occasionally evidence

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of allergic reaction to cigarette smoke is observed upon examination of the nasal passages.

All smokers have postnasal drip. The amount of drip varies with the type and number of cigarettes smoked, and the manner and frequency of the smoking. It is a fact, however, that the mucous secretion of the nasopharynx is affected by a single puff on the average cigarette. Convincing proof of this can be gained by a simple procedure. By using a nasopharyngoscope, it is possible to observe globules of mucus forming during the act of smoking.

It is not unusual to observe fluid in the submucous space of the uvula after heavy smoking. This edematous infiltration of the uvula is most conspicuous along its periphery. Increased vascularity and firmness of the uvula also is observed often in persons who have been smoking heavily for a long time. When affected acutely by the irritation of cigarette smoke, the blood vessels of the uvula become longer and dilated. Of interest also is the fact that after the smoking of most brands of cigarettes there is an increase in the number and size of the branches of the largest visible vessel. These observations must be made immediately after the smoking is done, for the blood vessels return to normal in 30 to 90 seconds.

The pharynx seems to be spared in a majority of smokers. As a rule, only persons who smoke two or more packages a day present increased redness of the posterior pharyngeal wall.

The larynx frequently shows anything from mild infection to tumor formation in heavy smokers. Hoarseness will appear in many of those who smoke excessively and who may be susceptible to the irritation of cigarette smoke. In 1950 the author described a condition of one or both vocal cords which was due to excessive smoking. This condition is known as "smoker's larynx";[10] its first manifestation is localized edema of one of the vocal cords, the sole symptom of which is hoarseness. If the patient stops smoking and rests his voice, the edema will disappear within 24 hours. If, however, he continues to smoke, fibrous tissue will be added to the edema so that the factor of permanency will be established. The lesion becomes an edematous fibroma. If smoking is continued, the other cord will be similarly affected. Since the edematous fibroma is permanent and no longer reversible, it must be removed as would any benign tumor. Among 180 cases of smoker's larynx observed by the author, all but 15 were in males. A great majority of the patients smoked two or more packages a day; only four smoked one package daily. The symptoms of edematous fibroma are hoarseness and vocal fatigue, the same that occur as a result of any small tumor of the vocal cord.

The author has carried out bronchoscopic examination of several patients immediately after they smoked a cigarette. Except for slight hyperemia of the trachea in one patient, nothing significant was seen.

Cough is encountered frequently among cigarette smokers. In a majority of cases it occurs upon awakening in the morning. This symptom is probably caused by localized edema or by accumulation of mucus in the trachea, or both. In persons who smoke very heavily, chronic bronchitis and even bronchiectasis can be traced to the smoking habit. In a number of cases observed by the author cough due to smoking abated when the patient switched to one of the filter-tipped cigarettes.

The irritation caused by the smoke of a cigarette bears a direct relation to the volume and density of the smoke that is generated. The volume and density increase with each puff; the shorter the cigarette becomes, the greater will be the volume and density of the smoke, and the greater the irritation. Filter tips, filter holders, and extra-length cigarettes favorably influence the volume and density of the smoke.

The author has been using a crude but dependable apparatus for testing cigarettes. It consists of an ear syringe to which is attached a glass Y tube. Two pieces of transparent tubing are attached to the arms of the Y tube. Into one end is placed a lighted cigarette; the other end is open. Since the volume of the syringe and the tubes through which the smoke passes is constant for each cigarette tested, a fairly accurate idea may be gained concerning the volume and density of the smoke that is generated by various types or brands of cigarettes. By compressing the open tube and pulling on the plunger of the syringe, smoke is drawn into the chamber of the syringe. The smoke is expelled by compressing the tubing which leads to the cigarette, while the other tube is left open. The distance from the butt end of the cigarette to the tip of the syringe is approximately seven inches, the same as that between the lips and the vocal cords of an adult.

The results of the clinical and laboratory tests carried out by the author were in accord with the results of the studies reported by the laboratories of the American Medical Association.[1] The results were in agreement as to which type of filter-tipped cigarettes and filter holders were most effective in reducing the stream of smoke.

The factors tending to reduce irritation favorably are filter tip, filter holder, extra length, compactness of tobacco and relatively high moisture content in tobacco. The factors tending to increase irritation are intensity of puff (inhaling), rapidity of smoking and closeness to butt.

Physicians are frequently called upon to advise patients concerning smoking. It is well to bear in mind that a great majority of patients are not

psychologically and emotionally able to voluntarily reduce the number of cigarettes they smoke. If smoking is harmful to a person, he will be served best if smoking is completely interdicted. Most smokers reduce the amount they smoke for a short period, but revert to their former habit of smoking in excess.

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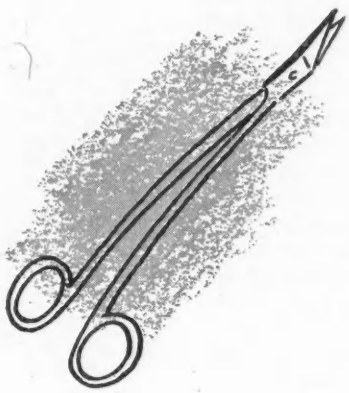

Absence of Coronary Thrombosis in Navajo Indians

JARVEY GILBERT, M.D., Burbank

• No proved case of coronary thrombosis was present among 10,267 admissions of full-blooded Navajos at the Navajo Medical Center in the years 1949-52. There were 125 cases of gallbladder disease in the same period.

Questioning of 100 patients elicited that the diets of many had an average or even high amount of cholesterol in them.

It was concluded that heredity is probably the most important factor in the prevention of coronary thrombosis in this select group.

WHILE MOST medical investigations deal with the presence of a disease, the present study deals with the absence of one—namely, coronary thrombosis.

In the course of a year of practicing medicine on the Navajo Indian Reservation in Arizona, where about 70,000 Navajo Indians live, the author noted that none of the patients he examined complained of typical anginal pain. Patients had pain in the chest from other causes but not from coronary artery disease.

The hospital records at the Navajo Medical Center, a general hospital, were reviewed for the years 1949-52, inclusive, and it was found that there were only five cases in which a diagnosis of coronary heart disease was made in a full-blooded Navajo. During that period there were 10,267 admissions of Navajos to this hospital. In none of the five cases of supposed coronary thrombosis (in which all the patients died) was autopsy done and in none was there electrocardiographic evidence of coronary disease. The diagnosis was made clinically only. Two of the patients, one 72 years of age and the other 80, died within 24 hours after admission, and coronary thrombosis was suspected but not proved. One other patient had syphilis and syphilitic heart disease. Two other patients died suddenly, and coronary disease was suspected. Therefore, there were no proved cases of coronary thrombosis during this four-year period and only five suspected cases among over 10,000 admissions to this general hospital. During this same period there were 60,405 out-patient visits and no case of coronary thrombosis.

Hospital records were also reviewed for the same period at St. Joseph's Hospital in Albuquerque, New Mexico, about 150 miles from the Navajo Medical Center. The number of admissions there, mostly of white persons, was 20,289, about twice the number at the Navajo Medical Center. There were, however, 146 cases of coronary thrombosis among them.

The Navajo people live to ages at which coronary artery disease develops in other persons (Table 1). Statistics from the Department of Interior show 10.4 per cent of the Navajo Indians are over 50 years of age, and 2.5 per cent over 70 years of age. The percentages of persons in the various age groups of the Navajos in general are comparable with the percentages in these age groups seen at the Medical Center.

From the Navajo Medical Center, Fort Defiance, Ariz.

Presented before a Joint Meeting of the Section on General Medicine of the California Medical Association and the California Heart Association at the 83rd Annual Session of the California Medical Association, Los Angeles, May 9-13, 1954.

A good deal has been written about the role of diet, particularly as related to cholesterol and fat intake, in the genesis of atherosclerosis.

Many Navajos eat the usual American diet with an average cholesterol intake. Many of the Navajo hospital workers eat normal diets. Many of the Navajos spend their childhood and adolescent years at boarding school eating normal diets. And many tuberculous patients have been hospitalized for years and have been given normal diets with average cholesterol intake. Several thousand served in the Armed Forces and ate normal diets.

Table 2 is a compilation of answers to a diet questionnaire given to 100 full-blooded Navajo patients. (No attempt was made to determine an "average" Navajo diet.) Patients were asked at what frequency they ate certain high-cholesterol foods. Of the 100, whose ages range from 25 to 80, 63 per cent were over 40 years of age and 33 per cent were over 50 years of age.

Some investigators believe that a low caloric intake or a starvation diet will prevent coronary disease. It is almost impossible to measure the caloric intake among the Navajos except in institutions. However, a study of the heights and weights of this group, although not perfect, is a good index of caloric intake. One hundred male out-patients over 30 years of age were measured and weighed with their clothes on. The average weight was 159 pounds with a variation from 102 pounds to 275 pounds. The average height was 67.45 inches with a range from 60 to 75 inches. The average weight of 100 females over 30 was 147 pounds, and the range was from 101 to 220 pounds. The average height for females was 62 inches and the range 56 to 67 inches.

Adelsburg and Zah,[1] studying 50 persons less than 46 years of age who died of coronary artery occlu-

TABLE 1.—*Data on age and sex of Navajos admitted to Navajo Medical Center 1949-1952*

Year	Sex			Ages			
	Male	Female	Total	1-19	20-49	50 and Over	Total
1949	1,064	1,371	2,435	1,151(47.3%)	996(40.9%)	288(11.8%)	2,435
1950	1,431	1,709	3,140	1,582(50.3%)	1,159(37.0%)	399(12.7%)	3,140
1951	1,174	1,527	2,701	1,343(49.7%)	1,043(38.6%)	315(11.5%)	2,701
1952	768	1,223	1,991	886(44.5%)	874(43.8%)	231(11.7%)	1,991

sion, found a striking familial occurrence. They also believed that a hereditary disturbance of lipid metabolism may be considered a predisposing factor in the genesis of some forms of atherosclerosis.

White[7] noted that in 27 per cent of the cases of a group of young patients who had coronary thrombosis, there was a history of coronary disease in one or both parents, whereas in a control group only 14 per cent had a similar history.

The *absence* of coronary disease among the Navajos suggests a strong hereditary factor.

During the period covered by this study (1949-52) a diagnosis of cholelithiasis or cholecystitis was made in 125 patients admitted to the same hospital. Thirty-five were males and 90 females. The diagnosis was confirmed by operation in 45 cases and made clinically or roentgenographically in the remainder. It was concluded that gallbladder disease is prevalent among the Navajos.

Joslin, among others, pointed out that the association of diseases of the gallbladder and coronary disease is striking. He also concluded that an excess of fat in the diet of diabetic persons may lead to the formation of gallstones. Beon[2] in 1937 attempted to show that cholelithiasis is due to some disturbance in the lipoid-cholesterol metabolism, which may also be at fault in atherosclerosis. Many observers believe gallbladder disease may damage the myocardium and thereby initiate changes in the coronary vessels. It has been shown that a high percentage of gallstones are composed of cholesterol.

In over 1,400 necropsies Breyfogle[3] noted a positive association between gallbladder disease and coronary disease when coronary disease was the direct cause of death.

Tenant and Zimmerman[6] in 1,600 autopsies found a significant association between heart disease in general and gallbladder disease. Miller[4] in 1932 noted that coronary thrombosis occurred more frequently in the presence of gallbladder disease. Schwartz and Herman[5] noted that cardiac disease was higher in the presence of cholecystitis.

It is fairly generally accepted that there is a relationship between gallbladder disease and coronary artery disease. Yet at the Navajo Medical Center no relationship was noted between these two diseases. There was absence of coronary disease and prevalence of gallbladder disease in this select group.

It is logical to assume that persons who will seek medical care for gallbladder pain would also seek care for pain of coronary occlusion, and as only a small proportion of persons die following a first coronary occlusion, these people, if they had had pain from coronary disease, would live long enough to seek medical care.

TABLE 2.—*Frequency of ingestion of some high-cholesterol foods by Navajos (as determined by questioning 100 patients in hospital)*

Food	Twice a Day or More	Daily or More	At Least Twice Per Week
Meat	20%	45%	66%
Lard	39%	76%	84%
Eggs	1%	17%	41%
Butter	2%	11%	21%
Milk	9%	32%	41%

Why do full-blooded Navajo Indians not have coronary disease? No definite answer can be given to this question. One would expect to see some coronary occlusion among so large a group of people if heredity were not an important factor. It is known that some animals can on any diet keep cholesterol levels down. No one has shown a direct relationship between cholesterol and atherosclerosis, and hypercholesteremia is not essential for the development of atherosclerosis in man.

From this study one can possibly feel that a constitutional or hereditary predisposition must be present for the formation of atherosclerotic disease —that the individual must be susceptible. The Navajo, it may be conjectured, is not susceptible, can eat anything and can live any way he wishes, and will not get coronary artery disease.

Navajos almost never become bald. They have practically no hair on the chest or the sides of the face. They are different outwardly, probably because of heredity, and probably are also different inwardly.

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X-ray, Malpractice and the Garrulous Physician

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FOR SOME UNKNOWN REASON, many physicians feel that they must know all of medicine. So many physicians dread the phrase, "I don't know," so avidly that it has fallen from their lexicon due to atrophy of disuse. When a malpractice suit arises, we all suffer by lowered respect for the only truly ethical profession, business or trade in the world today. Also, we are damaged by increased malpractice insurance premiums and by increased temptation to patients to file such actions. While it is agreed that the patient damaged by negligence of a physician should be entitled to recover just damages, all experts agree that most suits are filed unjustly.

Furthermore, most malpractice actions stem from statements by other physicians. Those authorities who are charitable blame such incidents on a raised eyebrow or a quizzical look. It might be better to place the blame squarely where it belongs—on definite statements made by physicians on subjects of which they know little or nothing. Some use this technique to impress the patient with their own ability and greatness.

Today I received a letter from a surgeon. He states that he is now treating one of my former patients. In writing, he blames jaundice that he claims that the patient developed on x-ray therapy administered to the patient's lip for a localized plaque of leukoplakia. Although he suggested a new etiology for icterus, the surgeon failed to enrich medical knowledge by an explanation of the mechanism of this occurrence. However, this is not as unusual as one might think. According to statements I have heard, x-ray has been blamed for everything from miscarriages to twins.

Other sad happenings come to mind. A patient with lichen planus of the lip received one x-ray treatment of 60r units with a half-value layer of 0.67 mm. of aluminum. Unfortunately, the lichen planus spread into her mouth. Three dentists and a general practitioner made unequivocal diagnoses of an "x-ray burn" of the mouth to the patient. If the patient had been approached by an unscrupulous attorney, an irritating law suit might have developed.

Another patient received three weekly treatments for psoriasis of the scalp of 60r each with the same factors mentioned previously. Conjunctivitis developed several weeks later. He had no difficulty inducing lawyer after lawyer to take the case as soon as he mentioned x-ray treatments.

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The reason for mentioning these incidents, experiences which are all too common to all dermatologists, is to introduce an explanation of the dangers of x-ray therapy. X-rays can cause burns. Chronic radiodermatitis can lead to the development of squamous-cell cancers. Most dermatologists practicing in the first decade of this century developed radiodermatitis themselves. Many of the pioneer dermatologists have been deformed by exposure to these rays and by the plastic procedures used to eliminate these dangerous hazards to life. Some of these men died from the harmful effects of radiation. Recently, I saw a patient die from malignant degeneration in radiodermatitis—the x-ray having been administered for psoriasis, a truly benign dermatosis. Dermatologists see more x-ray dermatitis than all the rest of physicians put together. No one is more cognizant of the dangers inherent in these rays. Yet, it should be remembered that dermatologists give more superficial x-ray therapy than the remainder of the medical profession.

No one refuses to ride in an automobile today because of the possibility of accidents. Knowledge and familiarity have established the safety of such vehicles if they are handled carefully. The reader can be assured that x-ray therapy is much safer than driving an automobile and the safety factors are much greater.

There is no medicine that cannot do harm. The minimum lethal dose of most agents is established before they are placed on the market. In other words, if enough of one of these medications is administered, death will result. However, the margin between the therapeutic and lethal dose, known as the therapeutic index, may be great. While two aspirin tablets may relieve a headache, thirty would probably kill a patient. Why, then, should the potential dangers of x-ray treatments be given more attention than the toxicity of aspirin? Actually, x-ray is much safer than aspirin. A patient with hypersensitivity to salicylates might die from a single tablet of aspirin. This does not occur with radiotherapy. While tolerance varies, there is no real idiosyncrasy to roentgen rays.

X-rays are carefully measured. The machines have many safeguards built into them. The modern machines are shock-proof. They have automatic timers. The tolerated dose is well known. No one gets an x-ray burn from 50 to 100r units. The amount that will cause radiodermatitis is not ap-

proached by the careful dermatologist or radiologist unless he is treating a malignant lesion. I have not seen radiodermatitis produced by a dermatologist in the past 15 years. Sulzberger[1] and his coworkers have shown that dermatologic dosage does not produce skin cancers even 25 years later.

Another point that should be remembered by the garrulous physician is that x-ray dermatitis can be diagnosed accurately both clinically and histologically. Therefore, if he makes such a diagnosis without adequate reason, he may find himself in court looking very very stupid in the eyes of patient, lawyer, jury and, even more important, his colleagues. Dermatitis may be due to locally applied medication. A scar may be due to biopsy or to trauma. Neither have the important connotations of an x-ray burn.

Legal complications have limited the value of x-ray therapy. The patient may resist its use. Many physicians fear x-ray treatments more than they do the Communists. I am told that x-ray epilation is shunned by dermatologists in Los Angeles for legal reasons despite the general acceptance that x-ray is the safest, quickest and surest method of treating tinea capitis. The infected child suffers because of the thoughtless statements of ignorant physicians, frightened patients and grasping lawyers.

While the popular lay "medical" writer has done a great deal to produce this pathologic fear of x-rays, medical schools must shoulder their part of the blame. They rightly stress the dangers of this modality but fail to emphasize the safety of this agent when administered by experienced experts with clinical judgment.

Therefore, remember that x-ray therapy is not the invention of the devil. Roentgen and Curie must be revolving rapidly in their graves if they know the appreciation given to their discoveries. It is the most valuable tool known for the treatment of dermatologic conditions. It is safe in the hands of an expert. If you think that a patient has been harmed by x-rays, better get a consultation before you start diagnosing and talking. It will save *you*, as well as the radiologist or dermatologist a great deal of unwarranted trouble.

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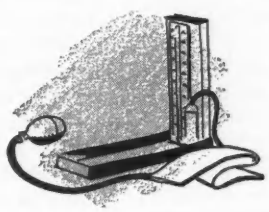

Cardiac Screening Procedures

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• *Seven per cent of a sample group of civil service employees were found to have diagnosable heart disease. The diagnosis was made on the basis of a complete physical examination and history taken by a specialist in internal medicine and/or heart disease. In addition a questionnaire form related to symptoms of heart disease was filled out by the patient, and various laboratory tests were made.*

As a technique in cardiac case-finding, the electrocardiogram was the best single device. Of all the cases of heart disease in this survey 65 per cent were detected from tracings obtained by using all 12 leads, and 57 per cent if only the three standard limb leads were taken; but of the presumably normal persons, 13 per cent would be erroneously suspected of possible heart disease by this technique.

Heart disease was detected in 50 per cent of the diagnosed cases on the basis of answers to three of the questions in the questionnaire. Eighteen per cent of normal persons would also have been suspected of having heart disease by this case-finding device.

Although the survey reported did not develop a simple cardiac case-finding technique, the data presented indicated that a questionnaire history-form, if judiciously used and evaluated, may be of value to physicians who examine large numbers of patients who are unwilling to submit to a complete cardiac evaluation.

DURING THE PAST five years the Los Angeles City Health Department has been conducting a Cardiac Case-Finding Program among Los Angeles City employees. The program embraced examination of 2,252 persons (1,859 men and 393 women) taken at random from the city payroll. The mean age of the subjects at the beginning of the study was 43.7 years. There were only 327 persons under the age of 30. To date the employees in the group have been subjected to three complete examinations spaced 12 to 18 months apart. The examinations were done by competent cardiologists and internists. Each person was examined by at least two different physicians over the years. The third examination has just been completed and the data are not completely compiled as yet.

There were many facets to the cardiac survey program. One purpose was to determine the most practical means, suitable for mass application, for the detection of heart disease. The primary purpose of all screening tests is to bring persons with disease to their physicians at an early stage and thus aid in the prevention of disabling complications. Although cardiac case-finding programs have been criticized on the grounds that too little can be done for patients with recognizable heart disease, the day may be near when effective measures for control and prevention of progressive heart disease will be available to all practitioners of medicine. The purpose of this report is to present, in a preliminary form, some of the results, difficulties and successes in the search by the Los Angeles City Health Department for a simple, effective cardiac case-finding technique.

Each subject on the survey answered a questionnaire as to history of symptoms associated with heart disease and was then seen by a physician who obtained a medical history. Complete physical examination (excluding rectal and pelvic) was made. Each person was subjected to the following tests: (1) a 12- or 13-lead electrocardiogram, (2) fluoroscopic examination of the chest, (3) electrokymogram, (4) 70 mm. minifilm of the chest, (5) determination of the vital capacity of the lungs, (6) urinalysis, (7) complete blood cell count, (8) sedimentation rate, (9) hematocrit, (10) serologic test for syphilis, (11) serum cholesterol, and (12) blood-sugar content (fasting). In addition, serum lipoprotein determinations on all persons 40 years of age and older were made by Dr. John Gofman at the University of California. Through the courtesy of Dr. Paul Starr of the University of Southern California, at least one protein-bound iodine determination was made for each subject. All observations were recorded on International Business Machine cards for statistical tabulation. The results of the first examination have been reported elsewhere.[1]

It was surprising to note, upon first examination, that 7.2 per cent of the subjects had demonstrable heart disease. Only one third of these patients had previous knowledge of their heart disease. In the subsequent examinations the percentage was practically the same (7.25 per cent). There was an 8 per cent decrease in the number of subjects between

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examinations, due to deaths, refusals to return and failure to locate individuals. Nevertheless, the percentage of heart disease remained constant each time because of the development of new cases between examinations. In all the examinations approximately 4 per cent of the subjects were classified as having "potential" heart disease or "possible" heart disease.

Hypertensive heart disease was the most common type (approximately 45 per cent of all cases). Coronary arteriosclerotic was next, comprising approximately 40 per cent. Third was rheumatic heart disease—about 15 per cent. Occasional cases of syphilitic heart disease, chronic cor pulmonale and congenital heart disease were diagnosed. In addition, there was a group of ten patients with pericarditis[2] and five patients with cardiomegaly without demonstrable cause.

RESULTS WITH VARIOUS TECHNIQUES

The blood tests, urinalysis and vital capacity determinations did not contribute to cardiac case-finding. A preliminary analysis of the patients with cardiac disease who had the Gofman lipoprotein determinations was inconclusive but suggested that there is no significant difference between the mean levels of the lipoproteins in persons with heart disease and those without.

In approximately 80 per cent of the cases in which heart disease was diagnosed, suspicion of heart disease was aroused by patients' answers to the previously mentioned questionnaire history-form. Ninety-four per cent of those with coronary arteriosclerotic heart disease, 60 per cent of those with rheumatic heart disease and 52 per cent of those with hypertensive heart disease had a "positive" history. Of those in whom heart disease was diagnosed, 33.7 per cent had previous knowledge that they had heart disease. Omitting these cases, the history-form was indicative of heart disease in only 62 per cent of the cases diagnosed. However, 31 per cent of the subjects without heart disease also answered one or more questions "positively." The large number of apparently "false-positives" would make such a screening technique invalid. Analysis of the individual questions suggests that three of them, as a unit, are reasonably sensitive and specific. This raises the possibility that further experience with questionnaire histories may develop additional sensitive and specific questions.

The following questions were asked at the time of the first examination: The first question, "Can you walk a reasonable distance out of doors without trouble?" was insensitive. Only 7.5 per cent of patients with cardiac disease and 1.3 per cent of presumably normal patients answered "no" to this question.

The second question, "Do you ever have distress, pain or an uncomfortable feeling in the chest while walking on the street or up inclines or steps?" was answered "yes" by 33.3 per cent of patients with cardiac disease and by 4.5 per cent of apparently normal persons.

Question Three, "While walking, are you forced to stop in order to rest?" was answered "yes" by 20 per cent of patients with cardiac disease and 2.8 per cent of normal persons.

Question Four, "Have you noticed increasing or undue shortness of breath with exertion?" was answered "yes" by 44 per cent of persons with heart disease and by 17 per cent of normal persons. The value of this question was depreciated by the large number of "false-positives." It was of interest that the percentage of affirmative answers to this question increased with age. Thirty-three per cent of all persons over 60 years of age, 27 per cent between 50 and 59 years, 19 per cent between 40 and 49 years, 12 per cent between 30 and 39 years and 8 per cent between 20 and 29 years answered "yes." Comparing these figures with percentages of diagnosed heart disease, it was clear that the percentage of false-positive answers to Question Four was highest in persons over 39 years of age. Hence, a history of increasing shortness of breath is more important as a screening device in the younger age groups.

Question Five, "Is your sleep disturbed because of coughing spells, difficulty in breathing when lying flat, asthmatic attacks, or choking sensation in the chest?" was insensitive and nonspecific. Only 6 per cent of patients with heart disease answered this question affirmatively.

Question Six, "Have you ever had palpitation of the heart?" was also of little value. Of the patients with heart disease, 25.6 per cent answered "yes" while 10.8 per cent of normal persons also answered "yes."

Question Seven, "Are your ankles swollen at bedtime?" was of no value in this survey. Of the patients with cardiac disease, only 8.8 per cent answered "yes," and 4.2 per cent of the normal subjects also answered "yes."

Analysis of questions 2, 3 and 4 showed that as a group, 50 per cent of the subjects with heart disease answered one or more of these questions affirmatively and that 18 per cent of the presumably normal persons also gave a "positive" answer. In summary, while the history-form relative to symptoms of cardiac disease assisted in the diagnosis of 62.5 per cent of the cases of heart disease diagnosed, 31 per cent of "normal" persons would have been suspect also. Questions 2, 3 and 4, as a group, reduced the false-positives from 31 per cent to 18 per cent but also reduced the true positives from 62 per cent to 50 per cent. In the second and third examinations,

questions 2, 3 and 4, as a group, showed comparable results.

At each examination the number of abnormal electrocardiograms was slightly more than 400; the range was from 410 to 420. In all three examinations the electrocardiogram was diagnostic or suggestive of heart disease in approximately 65 per cent of the patients with heart disease. In each examination approximately 13 per cent of presumably normal persons had abnormal electrocardiograms. If only the three standard limb leads were interpreted, the sensitivity of the electrocardiogram in case-finding would have been reduced to approximately 57 per cent. This indicates that the three standard limb leads alone have some value in case-finding in mass screening programs.

The electrocardiogram and the history-form did not "detect" cases of the same type. The electrocardiogram was most valuable in detecting hypertensive heart disease; the history-form was best in detecting coronary arteriosclerotic heart disease. The three questions (items 2, 3 and 4 in the questionnaire history-form) plus the three standard limb leads of the electrocardiogram "detected" 92 per cent of all cases, but 35 per cent of normal persons had either abnormalities in the three standard lead electrocardiogram or gave a "positive" answer to one of the three questions.

The electrokymogram and the minifilm were of no value in detecting heart disease. The questionnaire, physical examination, electrocardiogram and fluoroscopy contributed about equally to the diagnosis. The physical examination and fluoroscopy were also free from "false-positives." However, these two techniques (physical examination and fluoroscopy performed by specialists) are not suitable for mass screening in the detection of heart disease. Furthermore, they are insensitive in the detection of coronary arteriosclerotic heart disease, which is of rather high incidence in the adult population and which constituted approximately 40 per cent of the cases in the present series.

It is clear that an effective screening program for the detection of heart disease has not been devised as yet. The present study indicated that if only the three-lead electrocardiogram were used, only 57 per cent of cases of heart disease would be detected, while at least 13 per cent of normal persons would be erroneously suspected of heart disease. If only the questions 2, 3 and 4 of the history form were used, 50 per cent of cases would be detected while 18 per cent of normal persons would be suspected of possible heart disease. If both the three-question history form and the three-lead electrocardiogram were used, 92 per cent of cases of heart disease would be diagnosed but more than one-third of normal persons would also be suspect. However, this report may be of value to general practitioners, industrial physicians and others who examine large numbers of patients for specific problems not related to heart disease. Often such patients are unwilling to submit to a cardiac evaluation, which of necessity includes a complete history and physical examination. Perhaps a questionnaire history-form could be utilized by such practitioners to detect at least a significant fraction of cases of heart disease among their presumably well patients. Such screening devices must be controlled and understood by the physicians using them. Otherwise more harm than good will come of them because of the large number of false-positives. Any screening technique, and especially any for heart disease, is fraught with the danger of inducing iatrogenic disease.

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CASE REPORTS

Radioactive Iodine Therapy in Euthyroid Cardiac Patient

With Previous Mitral Commissurotomy

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THE PROBLEM OF TREATING a patient with rheumatic heart disease and intractable cardiac failure and embolization was met first by mitral commissurotomy, appendagectomy and evacuation of the auricular clots. But the end results of mitral commissurotomy are not always successful, even though the clinical reasons for performing it are valid. Although the threat of further embolic phenomena was abated by this surgical procedure, fracturing the tight stenotic valve did not improve the clinical status of the patient. Therefore, radioactive iodine was employed to reduce the patient to relative hypothyroidism in an endeavor to control the persistent right and left ventricular failure. The successful use of radioactive iodine in patients with severe cardiac disease whose thyroid function is normal has already been the subject of previous reports,[1-6] and experience in this form of therapy is increasing. The case reported here is unique in that two major cardiac procedures were combined, for the first time, to rehabilitate a cardiac cripple.

REPORT OF A CASE

The patient, a Caucasian woman, was first observed in April 1945, when her age was 42 years. In her history were recurrent tonsillitis in childhood and hemorrhoidectomy in 1933. For as long as she could remember she had had aerophagia with resultant belching, worse in recent weeks. The menstrual periods were normal, and there had been no menopausal symptoms other than nervousness for some two years. The basal metabolic rate was reported as —10 and —8. An electrocardiogram was within normal limits except for a prolonged QRST wave.

The patient was next seen in March 1947 with complaint of nervousness and of tightness and pain in the throat, radiating to the ears. The blood pressure was 140/80 mm. of mercury. The heart appeared normal. The body weight was 183 pounds, and the patient was put on a 1,000 calorie diet. Vitamin B complex and a half tablet of Dexedrine® twice daily were prescribed.

Five days later during an office visit, she complained of the same symptoms, plus a thumping in the throat which could be initiated by effort. The pulse and apical rate were grossly irregular, and an electrocardiogram showed auricular fibrillation with an apical rate of 130 to 150. The blood pressure was essentially unchanged from the previous week. Pressure on the carotid sinus slowed the rate but did not convert the rhythm. The circulation time of Macasol® was 30 seconds arm-to-tongue and 50 seconds arm-to-hand. Therapy was continued as before, and when examined a few days later the patient had sinus rhythm. In a roentgenogram of the chest the cardiac silhouette was normal. The basal metabolism rate was —13 and —10.

Fibrillation recurred toward the end of April 1947, and the patient was admitted to the hospital April 28. Quinidine given before hospitalization aborted the attack. On admission, the rhythm was sinus with occasional extra systoles, but there were systolic murmurs at the mitral and pulmonary areas, the latter being transmitted down the left sternal border. The lungs were clear, but, on inspiration, the edge of the liver was felt. There was no peripheral edema. An x-ray film of the chest showed moderate cardiac enlargement and a mitral configuration. In the gastric analysis, only absence of free acid was notable. Results of routine blood examination and urinalysis were normal. An upper gastrointestinal series, examination with barium enema and an intravenous pyelogram were all normal. Bromsulfalein retention was 17 per cent. Plasma protein bound iodine was 5.4 micrograms per 100 cc. of blood, and the basal metabolism rate was —3 and —7. The condition was diagnosed as paroxysmal auricular fibrillation caused by rheumatic heart disease.

A year later, in April 1948, the patient was hospitalized again, with complaint of rapid irregular pounding of the heart and throbbing in the neck. The rhythm on admission was sinus, however, and the electrocardiograph recorded right axis deviation, auricular hypertrophy and Grade I heart block (P-R, 0.20). An x-ray film of the chest showed that the heart had enlarged somewhat since the film taken a year before. Mitral configuration was still present, and in addition some passive pulmonary

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congestion was noted. The edge of the liver was palpated one finger breadth below the costal margin. The lungs remained clear and there was no edema at the ankles. The patient was digitalized with Digitoxin® and a maintenance dose of 0.2 mg. daily was administered, as it was felt that steady fibrillation could be maintained better with Digitoxin than with quinidine, for repeated efforts to maintain conversion increased the discomfort. After she left the hospital, she was treated with Belladenal® and Amniotin.®

With this medication the patient got along fairly well until June 1948, at which time an episode of numbness and pain in both legs occurred, worse on the right, and leg pulses were absent. The diagnosis was embolus at the bifurcation with propagation or extension down the right extremity. Hospitalized again, the patient was treated with papaverine, morphine, dicoumarin and right lumbar sympathetic block. Response was good, particularly to the latter procedure, and when the patient was sent home after six days, there was return of some pulsation to the right ankle. At home she was maintained on dicoumarin, Pitkin's menstruum and Buerger's exercises.

In September 1948 cough developed and a roentgenogram showed much pulmonary congestion and increased bronchial markings. Administration of Mercuhydrin® was started and the patient continued to take it, along with crude liver, until January 1949, when a switch was made to Belladenal, phenobarbital and a salt-free diet.

An x-ray film of the chest in October 1949 showed some further increase in the size of the heart. The hemoglobin value in the blood was 64 per cent. Ferrous sulfate was given, caused gastrointestinal upset, and was discontinued. Treatment was continued with Mercuhydrin and crude liver.

In January 1950 the liver was noted to be huge, in spite of all therapy. At about this time prolongation of menses developed. Since there was much pelvic tenderness, the patient was admitted to the hospital and had dilatation, curettage and laparotomy. A right intraligamentary fibroid tumor (8 to 9 cm.) was found embedded deep to the right of the cul-de-sac and was removed. Supracervical hysterectomy also was done. The heart, when percussed, was noted to be enlarged and there was an apical systolic murmur. The edge of the liver was felt five fingerbreadths below the costal margin. As the hemoglobin content of the blood was 10.7 gm. per 100 cc. (69 per cent) a transfusion of 500 cc. of blood was given. In the electrocardiogram impure flutter and right axis shift were found, and an x-ray film of the chest showed considerable cardiac enlargement with mitral configuration and moderate passive pulmonary hyperemia. The transverse diameter of the heart, which had been 15.7 cm. in 1947 and 16.4 cm. in 1948, was 18.2 cm. Treated with digitoxin, Belladenal, Mercuhydrin, Thiomerin® and a low salt diet, the patient responded fairly well.

When she left the hospital, therapy was resumed with Mercuhydrin, Thiomerin and Digitoxin as before and was continued until December 1950 when she was admitted to the hospital for the fifth time. She had been found semi-stuporous on the stairway in her home, without evidence of paralysis or pathological Babinski signs. She did not recall the circumstances surrounding this episode, but her mind cleared spontaneously. Cerebral embolism was considered a possibility but was not definitely established. In the hospital, on rigid dietary restriction, the body weight decreased 9 pounds to 145 pounds in three days. The opinion was that the patient had had too much work and emotional strain and that she needed the regimen of restricted diet and medication. The hemoglobin value on this admission was 76 per cent. On discharge from the hospital, Mercuhydrin was given three times weekly.

In March 1951 an ovarian cyst which had been discovered three months earlier was noticeably enlarging, and the patient was sent to the hospital for operation. An electrocardiogram taken just before admission recorded right ventricular hypertrophy, auricular fibrillation and probably incomplete right bundle branch block. The hemoglobin content was 12.5 gm. per 100 cc. (81 per cent). A multilocular interligamentous left ovarian cyst was removed.

At home the patient took Mercuhydrin, 2 cc. once or twice weekly, plus Dexamyl.® She did well until September 1951, when she had an episode of nausea and vomiting, and was treated with sedation and niacin; and regular doses of vitamin B_{12} were given.

In October 1951, a radioactive iodine uptake study showed that the patient was euthyroid, the result being 16.9 per cent—within the normal range.

In December 1951 tachycardia, a rate of about 110, was noted. The patient said she had been in generally poor condition for the preceding month. Digitalis dosage was doubled and administration of quinidine was begun. The condition of the patient deteriorated. She was admitted to the hospital three days later with a pulse rate of 135 and right heart failure. The liver was down three fingerbreadths, and she had 1 plus pitting edema at the ankles. The hemoglobin content was 10.6 gm. per 100 cc. (68 per cent). There were a few erythrocytes and leukocytes in the urine. In the hospital redigitalization was carried out after a period of omission of digitalis to make sure intoxication was not present. A diastolic murmur was heard at the apex for the first time.

The patient was discharged after five days in the hospital and at home was maintained on Mercuhydrin, occasionally given intravenously. On two occasions the patient may have suffered small embolizations.

Because of the progressively deteriorating course, regardless of therapy, it was judged that the best procedure for the patient to undergo next was mitral commissurotomy. On February 12 mitral commissurotomy with appendagectomy and evacuation of a large clot was carried out, and 1,500 cc. of blood and 300 cc. of plasma were administered.

The postoperative course was relatively benign. The only complications were a cooling and a decrease of pulses in the left leg and right arm on the day following operation. Pulses gradually returned without specific therapy, and the patient was discharged on the tenth postoperative day. The course at home was stormy. Oxygen, morphine and Demerol® were given but cardiac failure was not controlled. One months after discharge from the hospital mild jaundice developed with tremendously enlarged liver due to the pronounced cardiac failure.

The heart appeared large in a roentgenogram after operation. Persisting dullness and fluid at the left base made exact determination of the size of the heart difficult.

The condition of the patient became aggravated when jaundice developed. In April 1952 the patient was given Mercuhydrin, digitoxin, Belladenal and corticotropin (ACTH). X-ray films of the chest on April 29, 1952, showed obliteration of the left costophrenic and cardiophrenic angles and haziness in the left lower lobe. It was still difficult to tell much about the size of the heart by x-ray examination.

Toward the end of May the patient was again hospitalized for uncontrollable nausea which had begun about the time jaundice had developed. Ten days prior to this admission she had been sent to a sanitarium for the same reasons, and with the poor dietary management resulting from the nausea plus the sedation that was given for it, the heart failure had become more pronounced. She had grades II to III presacral edema and a tachycardia of 112. An electrocardiogram showed ST and T changes suggestive of drug effect or metabolic disorder. Two days after admission, fever developed. Four serial blood cultures grew no pathogenic organisms. The patient was treated with corticotropin with temporary success, and the temperature finally subsided almost to normal without the cause ever being definitely determined.

The response of the patient to commissurotomy was not so favorable as the potential response, and it was decided after this last hospital admission that she should be given a course of radioactive iodine as a euthyroid cardiac patient. Radioactive iodine therapy was started July 17 and continued to August 21, 1952, for a total dose of 30 millicuries. In the meantime Mercuhydrin, Neohydrin® and other diuretics were administered.

A test on October 21, 1952, showed that the radioactive iodine uptake was 2.58 per cent—in the hypothyroid range. However, the patient had no clinical signs of myxedema at this time. The radioactive iodine uptake, rechecked December 9, 1952, was reported 1.69 per cent—in the low range—and clinical signs of myxedema began to appear. Thyroid therapy was started and the patient was maintained on thyroid extract, in addition to the former therapeutic regimen.

Three weeks after completion of the course of radioactive iodine, the patient began to improve. Oxygen no longer was necessary, the lung fields cleared, the liver edge receded. The patient became ambulatory. The cardiac rate slowed to 70. With returning strength the patient was able to resume simple household tasks. She even drove an automobile, although this activity was frowned upon.

On March 15, 1953, the patient was admitted to the hospital with belching, salivation, nausea, retching and constipation, but it was noted that these symptoms became severe following the reading of an article on the use of radioactive iodine in the treatment of cancer. At her request a complete examination was carried out and the patient was reassured that she had no neoplastic disease. At this admission the apical rate was 74, the blood pressure 108/70 mm. of mercury, the hemoglobin 10.4 gm. (67 per cent) per 100 cc. of blood, the erythrocyte count 4,600,000 per cu. mm. and the leukocyte count 6,200. Blood urea nitrogen, chlorides, sodium potassim, total proteins, albumin and globulin were all normal. Cholesterol was in the low normal range, indicative of good control of the hypothyroidism induced by radioactive iodine. In roentgenograms, the entire gastrointestinal tract was normal, and x-ray examination of the chest showed for the first time no further increase in cardiac size.

For the next year the patient remained compensated without difficulty, made a trip to Honolulu and recovered from a bout of right middle lobe pneumonia.

COMMENT

In the five months between mitral commissurotomy and the beginning of treatment with radioactive iodine, the patient's condition progressively deteriorated. On two occasions she was not expected to live 48 hours longer. Yet, as soon as a relative hypothyroid state was brought about by radioactive iodine this patient was noticeably rehabilitated. She was not given a new heart, but two gains were accomplished. The cardiac operation removed the threat of further embolization, and the induction of hypothyroidism decreased the strain upon the badly diseased heart. At the time of last report the patient had had 19 fairly comfortable months owing to the combination of relatively new surgical and medical cardiac therapies.

SUMMARY

A case is reported of a patient severely ill with cardiac disease who improved clinically when she was treated by a combination of cardiac operation and radioactive iodine.

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Listeria Monocytogenes Meningitis in an Infant

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FOLLOWING IS A REPORT of a case of meningitis due to an organism Listeria (Listerella) monocytogenes in an 18-day-old infant. As far as can be determined this is the forty-third such case reported in the literature.

The points of interest are the comparatively rare pathogenic agent, the presence of a deep dermoid sinus in the sacrococcygeal area as a possible site of entry of the infection, and the comparatively good general health maintained by the infant despite the seriousness of the disease.

REPORT OF A CASE

The patient was an 18-day-old female infant who was born by spontaneous vaginal delivery and weighed 8 pounds 12 ounces at birth. The neonatal course was smooth and the only finding of interest was a rather deep invagination of skin without granulation over the sacrococcygeal area. When discharged from the hospital on the seventh postpartum day the baby weighed 8 pounds 7 ounces.

She did very well at home until the eighteenth day when she became "fussy" and anorexic. Rectal temperature was 104° F. There was no convulsion, vomiting or diarrhea but the nasopharynx was inflamed. One million units of penicillin was given and the same amount on the following day, with no improvement. Mild nuchal rigidity was then noticed and spinal puncture was performed. The pressure was normal but the fluid was cloudy; it contained 1,735 leukocytes (36 per cent polymorphonuclear cells and 64 per cent lymphocytes); the sugar content was 41 mg. per 100 cc. There was a 1+ reaction to a Pandy test. Leukocytes in the blood numbered 39,550 per cu. mm. (9 per cent metamyelocytes, 24 per cent banded, 42 per cent segmented polymorphonuclear cells and 25 per cent lymphocytes). Results of urinalysis were within normal limits.

The infant was placed in oxygen and given Ringer's lactate solution by clysis containing sulfadiazine. Streptomycin was administered intramuscularly, 50 mg. every six hours; and 600,000 units of procaine penicillin was given at the same intervals. Other measures were sponge baths, daily administration of Darrow's solution by clysis and later by mouth, desoxycorticosterone acetate intramuscularly and acetylsalicylic acid. On the second day after the patient was admitted the temperature was normal and remained so during the remainder of the hospital stay. The vessels in the tympanic membranes in both ears appeared engorged. The reflexes were normal, the rigidity of the neck lessened, and the fontanelle was soft.

An organism morphologically resembling Listeria monocytogenes grew on a culture of spinal fluid and a specimen was sent to the State Bacteriology Laboratory, which confirmed the identity. The organism was sensitive to aureomycin, bacitracin, penicillin plus streptomycin, chloramphenicol, terramycin and erythromycin. It was only slightly sensitive to dihydrostreptomycin and not sensitive to polymyxin, sulfonamids or penicillin alone.

Administration of terramycin then was begun even though the patient was recovering under the therapy previously described. In a specimen of peripheral blood taken the fifth day, leukocytes numbered 17,650 per cu. mm. (4 per cent eosins, 16 per cent banded, 27 per cent segmented polymorphonuclear cells and 53 per cent lymphocytes).

A consultant who examined the deep sacrococcygeal sinus expressed the opinion that it was a deep congenital dermoid sinus and, since no exudate or granulation was present, was probably not the site of entry of the organism. He suggested the injection of indigo carmine per thecum and observation for drainage through the sinus, but this was not done at that time. No abnormality was noted in an x-ray film of the lumbosacral spine.

Seven days after entry the baby was clinically well and had been afebrile for four days. She was discharged with prescription of continuing use of terramycin.

The infant remained afebrile, ate well and gained weight but had considerable nasal mucus, rattling respirations and stridor. As congestion of the vessels of the right tympanic membrane continued, myringotomy was carried out. Hemolytic staphylococci grew on a culture of exudate from the middle ear. The stridor was due to excessive nasopharyngeal mucus and the rather persistent otitis media was finally cleared after prolonged administration of terramycin. At 11 and a half months the child was normally developed and in excellent health. The sacrococcygeal dimple remained well epithelialized and was not irritated.

THE ORGANISM

Listeria monocytogenes is the causative agent in rare cases of meningitis and in some infectious mononucleosis-like syndromes in man and in certain diseases in animals and poultry. (Incidentally the infant in the present case lived in a country home where there was a horse, a burro and a cow but no poultry.)

The bacterium is a Gram-positive bacillus, sluggishly motile with a "tumbling" or spiral movement. It is 0.5 micron in width and 1 to 2.5 microns in length and occurs singularly or in short chains.

Submitted June 17, 1954.

There is a rough and smooth colony form; it is nonspore forming and facultatively anerobic. It causes a characteristic fermentation of the various sugars and a specific antigenic structure. Infections in man and animals are world wide. Interest developed regarding the organism's possible role as a causative agent in infectious mononucleosis. At present there is no conclusive answer to this problem.

Care must be taken lest these organisms be confused with Belta hemolytic streptococci or be mistaken for diphtheroids. For specific identification, injection of the organisms into the conjunctival sac of rabbits produces severe conjunctivitis and corneal involvement.

COMMENT

The transmission of the organism from animals to man has been strongly suggested in the world-wide literature and there is reason to believe that these infections are more common than expected. It is interesting to speculate as to whether or not such infections will increase as the more common organisms are altered by antibiotics. In a number of other cases of meningitis the disease was suspected at first of being tuberculous in origin and only after extensive culture and repeated spinal puncture was it positively identified as L. monocytogenes.

In other cases reported the patients were successfully treated with chloramphenicol and streptomycin.

SUMMARY

A case of meningitis due to Listeria monocytogenes is reported. The organism should be suspected as the causative agent more often, especially in rural areas.

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Pulmonary Hydatid Disease

Report of a Case

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PULMONARY HYDATID DISEASE is frequently referred to in connection with cysts of the lungs. However, the condition is uncommon in this country; only 47 cases have been reported in the literature in the United States and Canada.[5] In the case herein reported the disease was correctly diagnosed preoperatively, owing to fortuitous information, and successful treatment was carried out.

The patient, a 47-year-old Russian woman who spoke very little English, was admitted to the Santa Fe Coast Lines Hospital, Los Angeles, on January 31, 1954. She had been ill for five days with cough, chills, fever and hemoptysis.

On examination it was observed that the patient was thin, poorly nourished and acutely ill. She was coughing and expectorating blood-stained purulent sputum, together with almost bright red blood. Increased vocal fremitus was noted and there was dullness to percussion over the lower part of the left side of the chest. Rales were heard in that area posteriorly and a few at the right base posteriorly.

Leukocytes numbered 7,450 per cu. mm. of blood, with 1 eosinophil reported in the differential count. The result of a serologic test for syphilis was positive. No tubercle bacilli were seen microscopically in the sputum, none grew on a culture and the result of guinea pig inoculation was negative. Cytologic examination of the sputum was carried out, and suspicion of malignant cells was reported.

From the Medical, Surgical, and Pathological Departments of the Santa Fe Coast Lines Hospital, Los Angeles.

Submitted May 20, 1954.

Upon x-ray examination of the chest, an area of increased density in the left middle lung field was noted (Figure 1). The density was irregular in outline and the edges were not clearly demarcated. It measured some 9 cm. in its greatest diameter and was interpreted as being either a tumor or loculated interlobar fluid. Further investigation included an attempt to aspirate material from the area in question, which proved unsuccessful. Bronchoscopic examination also was carried out but nothing of significance was seen.

Penicillin was administered and symptomatic treatment was carried out. The temperature decreased from 103° F. to normal in several days, and cough and hemoptysis also diminished. However, the conditions observed in the chest upon physical and roentgen examination were not changed.

Ten days after the patient was admitted exploratory thoracotomy was scheduled. However, it was learned through the patient's son, who spoke English, that the patient had resided in Persia for a number of years; that in the course of emigrating to this country an x-ray film of the chest had been made and the patient had been told that she had "water on the lung as large as a lemon." As soon as the son gave this information, an Echinococcus skin test (Casoni) was done and the result was strongly positive. A circulatory eosinophil count gave a value of 1,500 per cu. mm. Several days later, the chest film done in Persia (Figure 2) was submitted by the son and comparison with the films at the present admission revealed a similar lesion except that the lesion as seen in the earlier film was more circumscribed, the edges were sharply delineated, and the shape was definitely globular. A diagnosis of hydatid disease was hence arrived at.

Thoracotomy was carried out uneventfully on Feb. 16, 1954 (16 days after admission) and a thick-

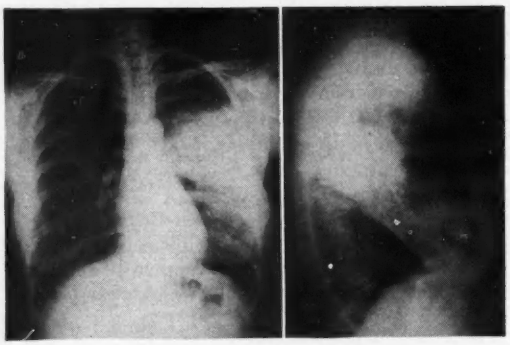

Figure 1.—Preoperative roentgenograms showing irregular area of increased density in left middle lung field.

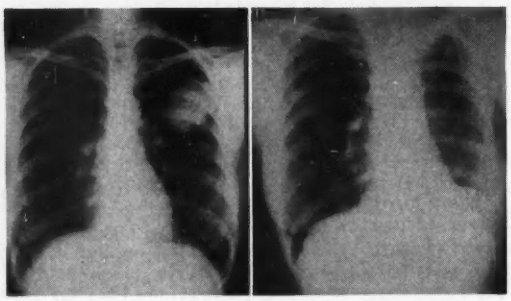

Figure 2.—*Left:* Roentgenograms taken in Persia two years before patient was examined for current illness. *Right:* Postoperative film.

walled cyst occupying the lower portion of the left upper lobe of the lung was observed. The affected lobe was removed and the cyst intact with it.

Pathologist's report. The specimen consisted of a resected segment of lung in which was embedded an oval cyst measuring 6.0 to 9.0 cm. in diameter. The cyst was unilocular. The lining, white and opaque, was 2 to 4 mm. in thickness. The contents of the cyst had been aspirated (for use as Casoni antigen) before fixation, but small brood capsules containing numerous scolices were found. The parenchyma of the lung surrounding the cyst showed considerable thickening and fibrosis for a distance of 1 to 2 cm. peripheral to the capsule.

The postoperative course was uneventful. On the fifteenth postoperative day, leukocytes numbered 8,000 per cu. mm. of blood and 23 per cent of them were eosinophils. The patient was discharged from the hospital on the sixteenth postoperative day. When observed on several occasions afterward she was well.

DISCUSSION

The symptoms of cough, fever and hemoptysis, which are typical of the disease, probably result from atelectasis and secondary infection of the lung parenchyma adjacent and distal to the cyst. These symptoms may also be caused by rupture of the cyst and the expectoration of its contents, with spontaneous cure or remission.[5] Rupture into a surrounding structure other than lung (pleura or pericardium for example) is a serious complication.

The physical signs are nonspecific. Laboratory data for the most part are also noncontributory. Eosinophilia, if encountered, might be of value. Similarly circulating eosinophil counts might also be expected to be elevated. Occasionally cyst fragments or scolices may be observed in microscopic examination of sputum. Aspiration of the cyst, as attempted in the present case, is contraindicated in view of the possibility of leakage occurring, which could result in anaphylaxis and possible dissemination of the lesion.

Roentgen demonstration of a persistent circumscribed mass of unknown cause in the lung parenchyma is undoubtedly the best clue for the diagnosis of this condition. Unfortunately, accompanying reaction in the lung surrounding the cyst may obscure the primary condition, as it did in the present case. X-ray examination of other structures—for example, bones or brain—may be considered to determine whether there are similar lesions elsewhere.

Further confirmation may be facilitated by the availability of antigen for the intradermal test of Casoni. Reports on the specificity of the test vary from a low percentage to the recent report of positive reaction in 25 of 29 proven cases.[1] Negative reaction to the test even in the presence of the disease is said to occur in early lesions. False positive reaction did not occur in a large series of proven cases.[3]

In the United States, most of the reported cases of hydatid disease were in persons who came from regions such as Argentina, Greece, Spain and Australia where cattle raising is common and dogs have access to the carcasses or entrails of the animals.[4]

The treatment of the condition is surgical. The procedures of marsupialization, lobectomy and pneumonectomy have been employed. The operative technique of enucleation, as described by Barrett and Thomas[2] in 71 cases, is probably the procedure of choice when possible.

SUMMARY

A case of pulmonary hydatid disease occurring in a patient who had lived in a region where this disease is prevalent is presented. The methods of diagnosis and treatment are outlined.

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Fixed Drug Eruptions

A Report of Two Cases, One Caused by Niacin, the Other by Cocaine

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FIXED ERUPTIONS have been recognized since the original report by Brocq[3] in 1894. Abramowitz[1] in 1941 reviewed the subject very thoroughly and listed the following drugs as having caused fixed eruptions:

- Acetanilid
- Acetylsalicylic acid
- Acriflavine
- Aminopyrine
- Antimony and potassium tartrate
- Antipyrine
- Arsenicals (acetylarsan, arsphenamines, mapharsen, tryparsamide)
- Barbiturates
- Bismuth salts
- Cinchophen
- Eucalyptus, oil of
- Iodides
- Ipomea
- Isacen
- Magnesium hydroxide (magnesia magma)
- Mercury
- Phenolphthalein
- Quinine
- Salicylates
- Sulfanilamide and its derivatives

Since then the list has been enlarged to include:

- Atabrine (mepacrine, quinacrine)[8, 9]
- Aureomycin[6, 13, 14]
- Benadryl (crossed fixed eruption with sulfanilamide)[5]
- Bromides[9]
- Diphenylhydantoin sodium (dilantin, phenytoin sodium)[2, 11]
- Penicillin[4, 10]
- Phenacetin[7, 9]
- Terramycin[6, 13]

This paper is presented to report additional causes of fixed eruptions.

CASE 1. A 37-year-old white secretary was first seen November 4, 1952, because of pruritic dermatitis of three or four weeks' duration. The patient had occasional migraine, for which she had been taking nicotinic acid since July of 1952. She also took Empirin Compound (acetophenetidin, acetylsalicylic acid, caffeine) at intervals, and secobarbital sodium.

There was an erythematous, papular and urticarial plaque on the ulnar aspect of the left wrist.

Dermatitis disappeared when all medication was discontinued. It was not reproduced by Empirin Compound or by secobarbital. Nicotinic acid, 50 mg. four times a day, repeatedly reproduced the eruption. The patient found that if she took 25 mg. four times a day the dermatitis did not appear. If she continued 25 mg. four times a day for three or four days, she could then increase to 50 mg. four times a day with only a moderate recurrence of the eruption, which appeared as erythema 15 minutes after ingestion of the drug and persisted for an hour or two.

CASE 2. A 36-year-old white schoolteacher was examined in December, 1945, because of a pruritic eruption of about 18 months' duration. There was a lichenified, erythematous, excoriated plaque on the posterior scrotum and the adjacent perineum. Clinically, the lesion resembled lichen simplex chronicus and was treated as such with crude coal tar ointment and x-ray therapy. The dermatitis improved somewhat but never cleared completely, although treatment was continued at intervals until October, 1946. The patient was subsequently observed because of another condition. At that time, questioning brought out that the dermatitis had continued until the summer of 1947; he had been symptom-free since except when he was given injections of procaine. Each injection, however small, was followed by pruritus and mild exacerbation of the dermatitis of the posterior scrotum and adjacent perineum. When the history of exacerbations with procaine was obtained, a check was made as to the therapy the patient was receiving at the time the dermatitis first appeared, and during the subsequent years, until the summer of 1947. The history showed that the dermatitis began shortly after treatment for sinusitis was instituted. The treatment was, for the most part, cocaine shrinkage of the mucous membrane and, occasionally, antrum washing. Treatment was begun in May of 1944 and continued until the summer of 1947. At times treatments were given as often as two or three a week, and occasionally as infrequently as once a month.

A single experimental cocaine shrinkage caused a minor amount of pruritus of only a few hours' duration. Neither an ointment of 1 per cent procaine nor 0.5 per cent cocaine rubbed into the area caused a reaction.

DISCUSSION

In Case 1, due to nicotinic acid, the lesion was a fixed eruption of pure urticarial type. The reaction gradually subsided although the patient continued to take the causative drug. The patient refused a request to increase the amount of nicotinic acid taken beyond 50 mg. four times a day because generalized flushing sometimes occurred on the dosage being taken.

In Case 2 the lesion was probably a fixed eruption of urticarial type, with, however, lichenification secondary to excoriation. Pruritus reappeared repeatedly after the injection of procaine. A mild attack occurred after experimental shrinkage of the nasal mucosa with cocaine. Neither cocaine nor procaine locally applied reproduced the symptoms.

A brief review of the literature on hypersensitivity to procaine and to cocaine leads to belief that cross-sensitization does occur.[12] Apparently the patient in Case 2 was capable of reacting to both procaine and cocaine, although only the latter was being used at the time the eruption appeared.

SUMMARY

Two new causes of fixed drug eruptions are reported: Nicotinic acid and cocaine. The eruption due to cocaine could be activated by the injection of procaine.

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Presented before the Section on Dermatology and Syphilology at the 83rd Annual Session of the California Medical Association, Los Angeles, May 9-13, 1954.

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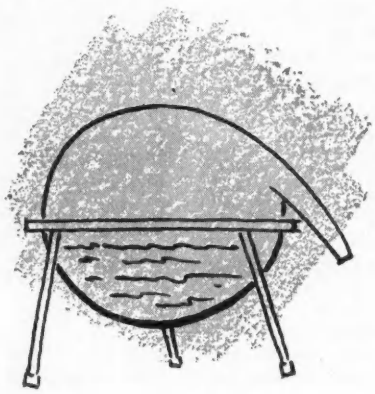

California MEDICINE

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EDITORIAL

The Physician and Community Service

COMMUNITY SERVICE is an historical function of the physician and of the medical profession. The service rendered by the physician to his patient is a basic service to an individual and to a community. When well rendered it is appreciated and it leads to good public relations, as the history of medicine attests.

The disturbing deterioration in medical public relations during recent years has perplexed many physicians. Curiously this deterioration has occurred during a period of unparalleled scientific achievement in medicine which one would expect to have an opposite effect. Perhaps these undeniably beneficial scientific advances have also had some undesirable side effects on the relations between the medical profession and the public. Perhaps the science of medicine is beginning to overshadow the all-important personal relationship between the individual physician and patient which is the cornerstone of traditional and effective medical practice. If so, this might account for a deterioration in medical public relations.

There is considerable evidence to support this conjecture. Physicians in training find the curriculum almost exclusively devoted to medical science. In practice they work in an atmosphere of the technical specialties. Many come to think of their patients as an example of a disease, rather than as a person with a disease. They tend to consider themselves mainly as technicians. Then, too, the public imagination is captured by each report of a new miraculous treatment or promise of imminent "conquest" of another disease by medical science. Consequently, there has arisen a clamor that these material marvels be mass-produced and mass-distributed, and that the technicians concerned be made to fall into line. This, after all, is the way our culture deals with a new and useful product.

Mass medicine has become an important issue. Many of its developments have been opposed by the medical profession, whose resistance has engendered misunderstanding and criticism in persons who have come to believe that scientific technology is the only really important element in medical practice.

Is mass medicine really good medicine for the human individual? This is a fundamental question which must be decided. The answer seems obvious. Mass medicine serves the individual best only in event of epidemic disease, of mass injuries such as occur in war, or of epidemic psychological disorder. It is inferior to individual personalized medicine in the treatment of endemic individual illness or injury with the accompanying complex psychic, somatic and environmental interrelationships. In ordinary practice the individual is best served by a trained and sympathetic physician who understands all the facets of his personal problem and who uses medical science as a tool. Experienced physicians know that this is true.

The impetus toward mass medicine is being abetted by other powerful forces. There is a worldwide ideological trend toward "security" at the expense of freedom. In this country collective action, even at the expense of certain important individual rights, has been accepted and given legal and judicial support. The development of "fringe" benefits has focussed attention on medical costs and medical insurance programs. The trend toward mass medicine has gained considerable momentum.

Physicians and the medical profession are clearly at a crossroads. They have been challenged to show why the mass production and mass distribution of

medical science is not superior to the traditional form of medical practice. Established truths have always had to be retested and reaffirmed if they are not to be displaced by newer ideas. This challenge of mass medicine is a serious one. In several countries it has all but displaced traditional medical practice, at least for a time. In our own country it has powerful supporters. The established truth must be reaffirmed and publicly recognized if it is to survive.

The essence of traditional medical practice is the service rendered by a physician to his patient and by the physician and the medical profession to the community. Through these traditional services the individual receives medical science tailored to fit his personal needs, and the community receives the greatest benefits. It is these services that must be strengthened, reemphasized and publicized along with the marvels of medical science through a program of public relations. A good public relations program serves to identify an individual, group, corporation, profession or the like with the true interests of the individual.

The term "community service" is widely used as a synonym for public relations when services rendered to an individual or to a community are provided. Such a program of publicized services can be highly effective public relations. The activities of physicians and of the medical profession easily fall within the scope of this term. Historically as well as today physicians are dedicated to the best interest of the individual. All that is necessary is that a program of professional and community service attuned to present-day needs be developed and maintained—and publicized.

Public interest in anything pertaining to medicine is great. And authoritative spokesmen representing a profession dedicated to the interests of the individual and supporting services to the community as a whole are usually heard and respected. An informed physician is a most effective public relations agent. A satisfied patient is another. An active program should highlight the services rendered and the motive behind them. It should result in renewed prestige for the physician and his profession, and should insure public support for those things which in the long run are truly important for the health and welfare of the individual and the community. The medical profession needs this support to carry on its work effectively.

LETTERS to the Editor . . .

I WOULD LIKE to write a rebuttal to the letter by Louis Shattuck Baer, M.D. (CALIFORNIA MEDICINE, Dec., 1954, pp. 420-421), in which he said that poliomyelitis patients requiring an iron lung should have been allowed to "mercifully die."

In October 1949 I suffered a severe attack of poliomyelitis, was placed in an iron lung, and today, five years later, I am still dependent upon this type of respiratory aid for an average of 16 hours per day. I have been a patient at Children's Hospital in San Francisco, and at Rancho Los Amigos Center in Los Angeles. This to establish my position as an observer of some experience with the problem.

I appreciate the writer's sincerity and his very obvious interest in this seemingly overwhelming problem. However, I believe that a good deal of what he says and concludes is the result of inferential thinking; more how he should imagine life would be in a mechanical respirator rather than how so living can be.

I am sure the possibility of such a life came so close to him that even now it is like a recurrent remembrance of a horrible nightmare. However, as in many things, the fear is worse than the actuality.

In the first place, it is clinically unacceptable to attach any importance to a patient's consent or lack of consent. In the terrible agony of the acute illness, gasping for breath, desperately ill in body and soul, but still grasping for the sweet remnants of life, no patient is sufficiently objective. In my case, I remember at the time faintly realizing the implications of the problem; but still I begged for the respirator. In my former practice I had seen patients in respirators for years, but at my time of desperation a breath of air was all that I considered. It does not seem to me that the decision rests with the physician. An iron lung is one of countless devices designed by the intelligence of man to prolong the life of the patient. To conclude that the particular life should not be prolonged by inferring that the patient would not want it so is again assuming a decision that we have traditionally left to the Creator.

I cannot agree with the rather materialistic philosophy implied in the remainder of the article. In light of the sympathetic concern shown, I know that it was not intentionally materialistic in outlook. The problem is really not "How can I feed myself?" or "How can I earn a living?" or "What will hap-

pen to my family?" These questions are of course real ones, and they plague us daily. The basic question, though, is "Can I be happy?" or "Is life worth living?" And, of course, these are the same questions that healthy persons must answer. I dare say that living in an iron lung considerably sharpens the focus and makes fuzzy, superficial thinking untenable! One must sharply dissect away the seemingly important things, the illusory standards and the petty apparent necessities which frequently encumber the average life and thought. The question must be faced decisively! "Is there a greater good than a greater evil?" No iron lung patient with whom I have talked has considered other than that the balance is for the good.

One's life is difficult; families and family relationships do suffer; one's hopes and dreams are destroyed but for a few; discomfort is always present, frustrations are maddening, and disappointments many. However, that is the evil.

Today I saw about a dozen patients in my office, within wheel-chair distance. I am important to them. We are having friends in for dinner with the family this evening. The table is a little crowded in front of the respirator, but the essences of good fellowship are still there, and the warmth of my family bustling about is as wonderful to me as to any man. I am as important and necessary to them as ever! Later this evening our friends will show us slides of their recent trip to Europe. Later on, I might play chess with my neighbor with insomnia, or perhaps work on an article which will deal with the relationship of poliomyelitis to allergy. Tomorrow, I will have to go into the lung early in order to come out for a couple of hours in the evening to meet with the executive committee of the local tuberculosis association. The next day is Wednesday, my day out of the office. A neighbor boy and my small son and I are going fishing on the wharf. It is almost an hour by wheelchair and an hour back, which leaves at least two hours for fishing; and then back into the lung. All the way down and back we will watch for the fall flights of the dragon-flies, and an occasional solitary vereo, and wonder that the buds of the black willows are beginning to swell already and it is only December.

Each patient must solve the problem of his own solitude and motivation. There are as many ways as there are patients.

The iron lung is, of course, still a damnable problem but it must not be solved with despair and pessimism, not of course with Pollyannaism, or obliqueness. As with the nuclear bomb, which we have also devised, we cannot be horrified by the Machine. We should feel responsible about its existence and for those who are directly affected by the necessity to live in an iron lung. There are many possible things that can be done. Being doctors does not exempt us from the responsibilities or the privileges of being human beings! We must use imagination, empathic concern, we must offer friendship and enjoy it, we must encourage, we must initiate a program for the patient as a living human being oppressed by a devastating and unremittent illness. First of all, means must be provided iron lung patients to live at home. Means must be provided by cooperative effort or, temporarily, by government subsidy, so that the patient can live with essential dignity. Psychological or psychiatric rehabilitation has been grossly neglected and is of greatest importance. Realistic employment rehabilitation is possible, and spontaneous community interest might even designate jobs which would eventually give independence. Switchboards can be operated by tongue or breath-control to make telephone answering services or physicians' exchanges possible for the iron lung patient. Specialty selling is being done with a small showroom and self-service, in conjunction with the iron lung. For persons with talent for it, creative writing is a most satisfying answer. The initiative must often come from the outside, but no community anywhere has failed to respond once the requirements have been effectively presented. The enormous resources of the record libraries for the blind should be made available to respirator patients.

The suffering which Dr. Baer imagines the machine to be causing is not because of the machine itself, but because of the isolation, the sense of social rejection, the erosion of the ego, the frequent necessity of going it alone. The invalided and the deformed and the disabled in mind and body will always be with us, as we know. There must be iron lungs, and braces, and mechanical kidneys, resectoscopes and all manner of useful mechanical contrivances, but our skill in technology must not find us incapable or insensitive in our essential concern for our fellow man. We must continue to care for him with skill, with loving kindness, with affirmation, and with patience. And this we must do not with lip-service but with actions, large or small.

I am glad that the correspondent is not restricted to an iron lung, but I am also grateful that I am still alive.

DUNCAN A. HOLBERT, M.D.

422 Locust Street
Santa Cruz, California

* * *

IN THE DECEMBER ISSUE of *California Medicine* appears a letter from Dr. Louis Shattuck Baer which states: "I will never give my doctor permission to place me in an iron lung. I would far rather die than risk being kept alive a total and permanent invalid."

Dr. Baer's statement deserves respectful reading for he faced this situation as a patient. It fails, how-

ever, to resolve the multihorned dilemma which confronts the physician who must decide upon the use of the respirator. It might do great harm if it caused the laity to believe that admission to the respirator is the end of all hope or if physicians should conclude therefrom that no useful purpose is served by the attempt to keep alive the adult or child with respiratory failure. It is not possible for the physician to know the ultimate fate of such a patient nor can he arrogantly decide whether or not the use of the respirator might be better for the given patient. The patient himself might choose which alternative to select if he were in a position to make a valid decision. Few parents would choose not to give a child the opportunity for survival even when there might be little assurance of eventual rehabilitation.

It is perfectly true that some patients with dismally profound respiratory paralysis are kept indefinitely alive by this machine in a state of complete dependency which offers no hope of ultimate recovery. Almost anyone, if he were to make his choice when he was well, would prefer death as a happier alternative. Unfortunately a course of action must be decided upon at a time when the patient's condition does not usually permit him to share in the decision and his previous convictions can hardly cause the physician to join in his determination for self destruction.

Even with prolonged and complete respirator dependence the will to live persists and many patients accomplish a surprisingly useful and happy existence.

There are many healthy persons who might prefer, before the emergency arises, not to subject their bodies to many of the indignities which accompany modern medical and surgical care. When these conditions actually occur the ultimate judgment for necessary care must be that of the physician.

It is almost impossible to determine during the rapid onset of respiratory failure which patients will go on to permanent dependency and which may quickly recover. The respirator was designed to maintain life during a short period of respiratory arrest with the hope that this function would return. As a matter of fact it was first devised for postdiphtheritic paralysis in which ultimate recovery might well be expected. Many patients who would certainly die during the height of poliomyelitis survive because of the use of the respirator and with varying degrees of postpolio paralysis. Some of these—and not an inconsiderable number—make complete functional recovery.

The first California respirator patient was twice unconscious from respiratory failure, once before he was admitted to the machine and a second time when he was removed for the substitution of another patient (no other machine being available) and before he could be readmitted. When last heard from this man was leading a useful life without very serious impairment. Examples might be multiplied of those who survived the height of the disease only because of the use of the mechanical respirator and have thereafter gone on to relatively normal existence.

The function of the physician is to try to prolong life to the best of his ability—his best efforts never afford more than a reprieve. It is not his prerogative to determine which patient should have the benefit of efforts to maintain life or when these efforts should be terminated. Such decisions must be other than his—sometimes that of a kindly providence.

Sincerely,

EDWARD B. SHAW, M.D.

San Francisco

* * *

THE DECEMBER ISSUE of *California Medicine* contained a letter by Dr. Louis Shattuck Baer presenting views concerning the use of the "iron lung" for respiratory assistance in poliomyelitis. If the point of view expressed by Dr. Baer were accepted by those of us who deal with acute poliomyelitis, the case fatality rate in this disease would return precipitously to that which prevailed ten years ago, and literally scores of unfortunate young people who now not only survive poliomyelitis but return to normal lives would be doomed to die. During the past four years, approximately 120 patients with severe bulbar and spinal respiratory paralysis have been treated in Alameda County hospitals. Of these, 15 have died. Since January 1953 some 50 patients with grave paralysis have been treated for respiratory paralysis and only one fatality occurred. No deaths have occurred during 1954. Of the 50 patients with respiratory paralysis treated during the past two years, only two are totally quadriplegic, and only a small additional number will remain very severely handicapped throughout life. Most of the patients involved have already returned to gainful lives, sufficiently rehabilitated to have resumed their normal family relationships and either their original or some other form of gainful employment. In virtually every instance, quite in contradistinction to Dr. Baer's opinion, *these patients would not have survived without the use of the iron lung.* Had some few of them been lucky enough to escape death, they would almost certainly have progressed to total quadriplegia as a secondary result of augmentation of damage to the nervous system through hypoxia.

Had we followed Dr. Baer's admonition to inform each of these patients of "all the pros and cons in-

volved" and permitted someone with Dr. Baer's views to prejudice the issue, the case fatality and recovery picture would undoubtedly have been quite different. Many of the patients were confused, acutely ill and quite beyond communication, let alone decision as to the best course to follow even had all the facts been given. As a matter of fact, in every instance where it was possible, a frank discussion of the procedures involved preceded the use of the respirator or the performance of tracheotomy. In no single instance was there any hesitation on the part of a well-informed patient to accept an obviously beneficial method of treatment.

In our experience, which parallels that in other centers, there are occasional psychological depressions among our seriously involved patients. There are frequent major problems of social and economic adjustment. However, it is the exceptional patient who ever expresses a distaste for life even in the face of extreme disability and dependence upon devices. The morale in ours as in all other respirator centers is exceptionally high. The utilization of the available techniques in psychology, physical therapy, occupational therapy, electronic implementation and good medical management opens up remarkable opportunities for living even among the most severely handicapped.

We should like to have an opportunity to demonstrate to Dr. Baer the actual situation among patients who survive the iron lung. In contrast to the pitiable condition described in his letter, particularly in his "reason number 5," the actual situation among some of the most handicapped might serve to alter his conviction. I should like to introduce him to one young man who still requires a portable respirator at night, who has no use of his upper extremities, yet who succeeds in teaching high school successfully and who looks upon his future as anything but hopeless. He might profit as well from the opportunity to discuss with a young professor of psychology the resources of the human spirit despite afflictions of motor apparatus including the power to breathe. He would have to be obdurate indeed to resist the infectious courage of patients from many northern California counties now under treatment at Fairmont Hospital who are making the fight toward rehabilitation which Dr. Baer seems to consider hardly worth the effort.

On the other hand, perhaps Dr. Baer's convictions with respect to euthanasia will prevent an objective appraisal of the facts. If this is so, he and others who hold similar views should reflect upon the ultimate consequences of their views.

While Dr. Baer does not frankly propose that the physician make a decision which might result in loss of life, he advises that doctors propagandize against the use of a life-saving measure among their patients while they are well. This curious doctrine is but one step from a policy of withholding treatment when, in the doctor's judgment, a life is not worth saving. The consequences of such a doctrine have been well illustrated in the recent past. Dr. Baer is urged to read an edifying if somewhat depressing article by Dr. Leo Alexander which appeared in the *New England Journal of Medicine*, 241:39-47, July 14, 1949. Entitled "Medical Science Under Dictatorship," it illustrates the pitfalls into which the physician may blunder once he rejects the most fundamental tenet of medical ethics—the duty to preserve human life.

Beyond this fundamental criticism of Dr. Baer's letter, it should be pointed out that his view is based upon a series of errors of fact. With specific reference to his "reasons for my decision never to allow myself to be placed in an iron lung (or rocking bed)," the following statements of fact are submitted:

1. Patients with partial paralysis of breathing muscles, if unsupported by respiratory aids, have a very great chance to develop complete quadriplegia and total respiratory paralysis leading to death.

2. Not only would these patients crippled by total or nearly total paralysis have mercifully died within a few hours, but so also would the 80 to 90 per cent of persons who make satisfactory recoveries following the use of the iron lung and other devices.

3. The physician would be ill advised indeed if he were to permit his critically ill patients, many of them mentally clouded by hypoxia, to decide the type of treatment necessary for their care.

4. It is true that the iron lung is keeping more and more people alive. In thirteen respirator centers across the country, most of which are equipped to provide care for fewer than twenty (rather than more than 100) patients, the rehabilitation rate is high and the great majority of patients treated return to their homes with relatively limited disabilities. Admittedly, a large number of severely disabled patients do accumulate over the years.

5. Those with the pitiable conditions described by Dr. Baer represent a challenge to the medical profession and allied disciplines which cannot be met by a defeatist attitude. The resources of human ingenuity can make life worth while even for them. The great momentum of the rehabilitation movement has been fostered to a great extent by remarkable achievements in the treatment of poliomyelitis.

6. The critical distinction between paralysis of the upper extremities and that of the lower extremities could not be sustained on the basis of Dr. Baer's philosophical doctrine. It is no great extension of

his point of view to deny care to persons handicapped by paraplegia as was the late Franklin Delano Roosevelt. The paraplegic may also be looked upon with pity rather than hope. Food as well as medical care could be denied him too, if we were to decide on the basis of emotion and personal reaction which patient should survive and which should not.

7. Dr. Baer's view that the degree of damage in poliomyelitis is entirely dependent upon the extent of virus invasion disregards the factor of hypoxia as an element in the spread of pathological process and a major factor influencing recovery. It is not true that the extent of involvement is determined by factors "beyond human ability to alter in any way." The diminishing frequency of quadriplegia, despite the vastly increased survival rate, is adequate testimony against this nihilistic viewpoint.

8. The family welfare of the patient stricken with severe poliomyelitis is subject to amelioration by a host of willing individuals and agencies. A civilized society such as ours can succeed in meeting this challenge very well. When it fails to do so, the fault may all too often be traced to a lack of conscientious endeavor on the part of those who supervise the care of the afflicted individuals.

I am confident that I speak for all of my fellow physicians who have devoted much energy to the solution of the problem of respiratory paralysis in poliomyelitis. I am equally confident that I speak for the great majority of those patients who have, through the grace of Providence, and the utilization of many remarkable "man-made machines" survived to face the continuing challenge of human endeavor.

LEON LEWIS, M.D.

Chief, Poliomyelitis Service
Poliomyelitis Respiratory and Rehabilitation Center, Fairmont Hospital, San Leandro.

California MEDICAL ASSOCIATION

NOTICES & REPORTS

Council Meeting Minutes

Tentative Draft: Minutes of the 409th Meeting of the Council, Los Angeles, December 11, 1954.

The meeting was called to order by Chairman Lum in Conference Room No. 2 of the Biltmore Hotel, Los Angeles, at 9:30 a.m., Saturday, December 11, 1954.

Roll Call:

Present were President Morrison, President-elect Shipman, Secretary Daniels, Speaker Charnock, Vice-Speaker Bailey and Councilors West, Wheeler, Loos, Sampson, Pearman, Randel, Ray, Sherman, Lum, Bostick, Teall, Frees, Carey, Kirchner, Reynolds, Varden and Heron.

Absent for cause, Editor Wilbur.

A quorum present and acting.

Present by invitation during all or a part of the meeting were Messrs. Hunton, Thomas, Gillette and Clancy of C.M.A. staff; legal counsel Howard Hassard; county society executive secretaries Bannister of Orange, Donovan of Santa Clara, Foster of Sacramento, Geisert of Kern, Jensen of Fresno, Nute of San Diego, Scheuber of Alameda-Contra Costa, Thompson of San Joaquin, Young of Los Angeles, and Robert Marvin of Riverside; Jerry L. Pettis of Los Angeles and Robert Williams of Orange County; Messrs. Ben H. Read and Eugene Salisbury of the Public Health League of California; Mr. K. L. Hamman of California Physicians' Service; Drs. H. L. Gartshore, Mathew Ross, James C. Doyle, J. Lafe Ludwig, J. Norman O'Neill, Murray Hunter Brown and Eugene F. Hoffman.

1. *Minutes for Approval:*

(a) On motion duly made and seconded, minutes of the 408th meeting of the Council, held October 3, 1954, were approved.

(b) On motion duly made and seconded, minutes of the 245th meeting of the Executive Committee, held November 17, 1954, were approved.

2. *Membership:*

(a) A report of membership as of December 9, 1954, was presented and ordered filed.

(b) On motion duly made and seconded in each instance, nine applicants were elected to Retired Membership. These were:

O. O. T. McAllister, Alameda-Contra Costa County; Hugh W. Bell, Kern County; George Martyn, Marie A. Vachout, Los Angeles County; William L. Garth, San Diego County; Lionel Player, Harry P. Robarts, Francis Williams, San Francisco County; Paul T. Quarry, Sonoma County.

(c) On motion duly made and seconded in each instance, 21 applicants were elected to Associate Membership. These were:

Leo J. Butler, Grace M. Hyde, Alameda-Contra Costa County; H. W. Bissonette, Richard V. Freeman, Lorna M. Forbes, Edmund B. Hardin, Leroy Hyde, Robert M. Lipschutz, Stefan P. Wilk, Los Angeles County; Loyd W. Bond, Paul W. Embree, Madera County; Isabella Clinton, Napa County; Bruce M. Summers, Riverside County; George A. Gross,

Norris R. Jones, John Pennington, George G. Snively, Charles M. Webster, Sacramento County; William B. Beach, Jr., N. L. Petrakis, Richard D. Walter, San Francisco County.

(d) On motion duly made and seconded in each instance, reductions of dues were voted for 13 applicants for reasons of illness or postgraduate study.

(e) On motion duly made and seconded, 58 members whose memberships had become delinquent, were voted reinstatement on payment of their dues.

(f) Report was made on an appeal received from a San Francisco member who was expelled from membership following hearing of charges of unprofessional conduct.

On nomination duly made and seconded, it was voted to appoint Dr. T. Eric Reynolds as a conciliator in this case.

On motion duly made and seconded, it was voted to hear the appeal during the next meeting of the Council to be held in San Francisco on Saturday, February 5, 1955, at 2:00 p.m.

3. *Financial:*

(a) A report of bank balances as of December 9, 1954, was received and ordered filed.

(b) A report of receipts and expenditures for November and for the five months ended November 30, 1954, was received and ordered filed.

4. *State Department of Public Health:*

Dr. Malcolm H. Merrill, State Director of Public Health, reported that state legislation will be needed to make state hospital construction fund laws coincide with amendments adopted by Congress to the federal Hill-Burton law. Legal counsel Hassard is reviewing state law amendments prepared by the Attorney General's office.

Dr. Merrill reported that the Association of State and Territorial Health Officers had voted to request that polio vaccine be confined by the National Foundation for Infantile Paralysis to use in first and second grade children and that pregnant women not be considered as additional recipients of the prospective 9,000,000 units. He also stated that the State Department of Public Health had been assigned to a study of the factors surrounding smog conditions. On motion duly made and seconded, it was voted that the Council recognizes that smog may constitute a serious health problem and for that reason the Council will lend assistance to any official agencies investigating the problem.

5. *Public Policy and Legislation:*

Discussion was held on a proposal of the State Department of Mental Hygiene for the establishment throughout the state of mental hygiene clinics. On motion duly made and seconded, this subject was voted referred to the Executive Committee for further study.

6. *Committee on Public Health and Public Agencies:*

Dr. Francis E. West, chairman of the Committee on Public Health and Public Agencies, reported that there are various problems concerning the use and distribution of gamma globulin and polio vaccine, discussion of which will come before a later meeting.

7. *Public Relations:*

(a) Ed Clancy reported that more than 1,000,000 pieces of literature produced by the Public Relations Department had been ordered by member physicians for distribution to their patients. In addition, more than 7,000 members have ordered a desk or wall plaque which invites a frank discussion of medical fees and services.

(b) A request from the San Francisco Medical Society for the appropriation of $865 for production of a television film was discussed. It was pointed out that a similar request for funds from another county society had been denied a year earlier. On motion duly made and seconded, it was voted to table the request pending the establishment of a policy to cover matters of this type.

8. *Conference on Physicians and Schools:*

Secretary Daniels reported on the success of the first Conference on Physicians and Schools, held in Fresno, November 11-12. He presented a series of recommendations adopted by the conference. The Council acted on these recommendations as follows:

(a) Moved, seconded and voted to approve a recommendation that the Association recommend to all Boards of Education periodical health examinations, including chest x-rays and pertinent laboratory work, for all school personnel, certificated or not and regardless of tenure status.

(b) Referred to the Committee on Public Health and Public Agencies a recommendation for development in general hospitals of preventive medical services for indigents.

(c) Referred to the same committee a proposed recommendation by the Association to the Joint Committee of the State Department of Public Health and the State Department of Education for the formulation of guides for the suggested development of local health policies and standing orders to be followed in emergency care.

(d) Approved the establishment of school health committees in the county societies; to work with others in solving problems of school health; referred to the Executive Committee the question of employing staff representatives for this purpose.

(e) Approved a request to the State Superinten-

dent of Public Instruction that two groups of school principals make the school health program their theme for 1955 meetings.

(f) Approved formation of a State Advisory School Health Council, with representation from other groups.

On motion duly made and seconded, it was voted to commend Dr. Daniels and Mr. Robert Thomas for having arranged and carried through an outstandingly successful conference.

9. *Rollen Waterson Associates:*

Mr. Waterson suggested that a special meeting of the House of Delegates, which had been urged as a means of discussing health insurance problems, was probably not needed at this time. On motion duly made and seconded, it was voted not to schedule such a meeting.

On motion duly made and seconded, it was voted that Rollen Waterson Associates be instructed to aid and counsel each county society in which pressure and urgency exist and which requests such counsel in discussing the $4,200-$6,000 income ceiling and fee schedule, to the end that such counties may better resolve their problems, and that this be one of their major activities.

Mr. Waterson also commented on the current findings in a survey which seeks to determine possible causes for patient dissatisfaction with physicians.

10. *Committee on Mental Health:*

Dr. H. L. Gartshore, chairman of the special Committee on Mental Health, reviewed the committee's report, stated that psychiatrists and clinical psychologists at the national level have suggested that no new legislation in the field of licensing or registering psychologists be undertaken by either group at this time, and suggested that a committee similar to the current committee be continued for purposes of discussion of this subject with the psychologists.

On motion duly made and seconded, it was voted to commend Dr. Gartshore and his committee for an excellent study and report.

11. *California Physicians' Service:*

Mr. K. L. Hamman reported that the C.P.S. membership is now more than 660,000 members and the physician membership more than 12,000. He stated that in the first ten months of 1954, a total of 271,000 members had been enrolled and that annual revenues from the nonveteran program is running at the rate of $25,000,000 annually. He also reported that the average hospital stay has risen from six to seven days in the past year. The indemnity insurance company is ready to do business, he said, and has received one request from a county society to issue contracts. The administrative expense of C.P.S. is now 11.9 per cent of dues received.

12. *Legal Department:*

Mr. Hassard reported that several proposed changes in the Medical Practice Act are contemplated in bills to be proposed by the Board of Medical Examiners.

Mr. Hassard also reported on proposed federal legislation relating to payments by states for the education of medical, dental and veterinary medical students in schools operated by other states. On motion duly made and seconded, it was voted to go on record as favoring the purpose of this legislation but to defer action on it until a more thorough study of the school facilities can be made.

On motion duly made and seconded, it was voted to favor the purpose of state legislation proposed by registered nurses to clarify present regulations governing physical therapy.

On motion duly made and seconded, it was voted to express the view that there is no present need for the establishment of a new licensing system to cover naturopaths.

13. *Medical Services Commission:*

Dr. Hollis L. Carey, chairman of the Medical Services Commission, introduced Dr. Frank J. Cox, who reported on the progress in a statewide relative value fee study. The fee subcommittee has retained Mr. Ralph Nelson as an actuary to assist in evaluating the study returns and has sought the further assistance of Frank Dickinson, Ph.D., director of the A.M.A. Bureau of Medical Economic Research. Dr. Dickinson spoke briefly on the further work needed to make the relative value fee study of value to all physicians.

Dr. Cox estimated that an additional $10,000 would be needed to carry on the additional studies, and on motion duly made and seconded, by more than a three-fourths vote of all voting members, it was voted to appropriate an additional $10,000 for this purpose.

14. *Annual Secretarial Conference:*

Secretary Daniels suggested that invitations to the annual Secretarial Conference be sent to all county society presidents and secretaries, to chairmen of medical services committees and to the presidents and secretaries of the branches of the Los Angeles County Medical Association. This suggestion was approved by the Council and the date of February 6, 1955, or January 30, 1955, was set for this conference.

15. *Sympathy to Mrs. J. Frank Doughty:*

On motion duly made and seconded, it was voted to express to Mrs. J. Frank Doughty the sympathy of the officers and Councilors in the death of her husband.

16. *Alternate Delegate to American Medical Association:*

On motion duly made and seconded, it was voted to elect Dr. Sidney J. Shipman as Alternate to Dr. Dwight L. Wilbur, Delegate to the A.M.A. This appointment will run for the calendar year 1955 and the office, to succeed the late J. Frank Doughty, will be set for election at the 1955 Annual Session.

17. *Crippled Children's Program:*

Dr. Hartzell Ray gave a progress report on meetings held with the State Department of Public Health and with osteopathic representatives for the discussion of possible recognition of osteopathic specialists in the treatment of crippled children's cases.

18. *Advisory Planning Committee:*

Mr. Hunton reported on the meeting a day earlier of the Advisory Planning Committee and requested the Council to name Mr. Robert Marvin of Riverside County and Mrs. Olive Neick of San Francisco as new members of the committee. On motion duly made and seconded, these appointments were approved.

19. *Foreign Tours:*

Mr. Hunton reported on three requests from travel companies or agencies for C.M.A. approval of proposed foreign tours. On motion duly made and seconded, it was voted to disapprove all such requests.

20. *Medical School Activities:*

On motion duly made and seconded, it was voted to refer to the Executive Committee several problems revolving around the private practice of medicine in publicly-supported medical schools and facilities.

21. *Osteopathy:*

A letter from Dr. Wayne Pollock, giving a progress report on meetings of his special committee with a similar committee of osteopaths on the subject of amalgamation, was read and ordered filed.

22. *Committee on Rural Health:*

Dr. Henry A. Randel, chairman of the Committee on Rural Health, reported on the Rural Health Conference planned for Fresno in February, stated that his committee was working with the statewide Rural Health Council and that the success of the conference would depend in large measure on the participation of physicians.

23. *Standing and Special Committees:*

Dr. Daniels commented on the need for revising policies in effect relating to standing and special committees and asked that this subject be taken up at a later meeting.

Adjournment:

There being no further business to come before it, the meeting was adjourned at 5:15 p.m.

DONALD D. LUM, M.D., *Chairman*
ALBERT C. DANIELS, M.D., *Secretary*

Executive Committee Minutes

Tentative Draft: Minutes of the 246th Meeting of the Executive Committee, Los Angeles, December 11, 1954.

The meeting was called to order by Chairman Heron in Conference Room No. 2 of the Biltmore Hotel, Los Angeles, at 5:15 p.m., Saturday, December 11, 1954.

Roll Call:

Present were President Morrison, President-elect Shipman, Speaker Charnock, Council Chairman Lum, Auditing Committee Chairman Heron and Secretary Daniels. Absent for cause, Editor Wilbur.

Present by invitation were Messrs. Thomas and Clancy of C.M.A. staff; legal counsel Hassard; Mr. Ben H. Read of the Public Health League of California; Rollen Waterson, health insurance consultant; and Drs. Murray Hunter Brown, J. Philip Sampson, Frederick G. Kirby and M. M. Horner.

1. *California Tuberculosis Association:*

On motion duly made and seconded, it was voted to support in principle the furnishing of adult educational facilities in tuberculosis sanitoria, subject to the furnishing of a copy of proposed legislation to the Committee on Public Policy and Legislation before final approval is given.

2. *Physicians' Benevolence Fund:*

Mr. Hassard presented for signatures the articles of incorporation of Physicians' Benevolence Corp., a California nonprofit corporation organized for charitable purposes. This corporation will take over the functions of the present Physicians' Benevolence Committee and will make possible the elimination of certain taxes.

3. *Insurance Representatives:*

Discussion was held on a request for a meeting with Association officials received from representatives of several insurance companies in the accident and health insurance field. It was agreed that such a meeting should be held at a later date.

Adjournment:

There being no further business to come before it, the meeting adjourned at 6:30 p.m.

IVAN C. HERON, M.D., *Chairman*
ALBERT C. DANIELS, M.D., *Secretary*

In Memoriam

BISHKOW, ISADORE E. Died in Los Angeles, October 12, 1954, aged 66, of hemorrhage from esophageal varices and cirrhosis of the liver. Graduate of the University of Illinois College of Medicine, Chicago, 1911. Licensed in California in 1911. Doctor Bishkow was a member of the Los Angeles County Medical Association.

✤

ENLOE, NEWTON T. Died in Chico, December 14, 1954, aged, 82, of bronchiectasis. Graduate of the Missouri Medical College, St. Louis, 1895. Licensed in California in 1901. Doctor Enloe was a member of the Butte-Glenn Medical Society.

✤

FLEMING, LUTHER P. Died in Sanger, December 30, 1954, aged 78, of bronchopneumonia. Graduate of Cooper Medical College, San Francisco, 1904. Licensed in California in 1904. Doctor Fleming was a member of the Fresno County Medical Society, a life member of the California Medical Association, and an associate member of the American Medical Association.

✤

GALLAGHER, VINCENT J. Died in Los Angeles, January 3, 1955, aged 60, of carcinoma of the lung. Graduate of St. Louis University School of Medicine, Missouri, 1918. Licensed in California in 1926. Doctor Gallagher was a member of the Los Angeles County Medical Association.

✤

GUNN, HERBERT. Died in San Francisco. December 23, 1954, aged 82. Graduate of Cooper Medical College, San Francisco, 1895. Licensed in California in 1896. Doctor Gunn was a retired member of the San Francisco Medical Society, the California Medical Association, and an associate member of the American Medical Association.

✤

JACOBSEN, JESS F. Died in San Francisco, December 19, 1954, aged 50, of coronary artery disease. Graduate of the University of California Medical School, Berkeley-San Francisco, 1935. Licensed in California in 1935. Doctor Jacobsen was a retired member of the San Francisco Medical Society, the California Medical Association, and an associate member of the American Medical Association.

KINYOUN, FLOYD H. Died in Santa Monica, December 23, 1954, aged 63. Graduate of Creighton University School of Medicine, Omaha, Neb., 1915. Licensed in California 1937. Doctor Kinyoun was a member of the Los Angeles County Medical Association.

✤

KOFF, RAPHAEL J. Died in Los Angeles, December 14, 1954, aged 44, of coronary artery disease. Graduate of the University of Minnesota Medical School, Minneapolis, 1935. Licensed in California in 1939. Doctor Koff was a member of the Los Angeles County Medical Association.

✤

LIPSON, BARNETT. Died November 12, 1954, aged 55. Graduate of McGill University Faculty of Medicine, Montreal, Quebec, 1928. Licensed in California in 1929. Doctor Lipson was a member of the Los Angeles County Medical Association.

✤

LYNCH, WILLIAM C. Died in Aptos, December 18, 1954, aged 67. Graduate of the Oakland College of Medicine and Surgery, 1915. Licensed in California in 1915. Doctor Lynch was a retired member of the San Mateo County Medical Society, the California Medical Association, and an associate member of the American Medical Association.

✤

MEYER, PAUL J. Died in San Francisco, December 21, 1954, aged 67. Graduate of Friedrich-Wilhelms-Universität, Medizinische Fakultät, Berlin, Prussia, Germany, 1912. Licensed in California in 1942. Doctor Meyer was a member of the San Francisco Medical Society.

✤

ROSE, ERNST. Died in San Francisco, December 27, 1954, aged 54. Graduate of Medizinische Fakultät der Universität, Wien, Germany, 1926. Licensed in California in 1938. Doctor Rose was a member of the San Francisco Medical Society.

✤

SWEETSER, GEORGE W. Died in Martinez, December 14, 1954, aged 75, of carcinoma of the pancreas. Graduate of the University of California Medical School, Berkeley-San Francisco, 1901. Licensed in California in 1901. Doctor Sweetser was a retired member of the Alameda-Contra Costa Medical Association, the California Medical Association, and an associate member of the American Medical Association.

APPLICATION FOR HOUSING ACCOMMODATIONS

FOR YOUR CONVENIENCE in making hotel reservations for the coming meeting of the **California Medical Association,** May 1-4, 1955, in San Francisco, hotels and their rates are at the right. Use the form at the bottom of this page, indicating your first and second choice. Because of the limited number of single rooms available, you will stand a much better chance of securing accommodations of your choice if your request calls for rooms to be occupied by two or more persons. **All requests for reservations must give definite date and hour of arrival as well as definite date and approximate hour of departure; also names and addresses of all occupants of hotel rooms must be included.**

ALL RESERVATIONS MUST BE RECEIVED BEFORE: APRIL 15, 1955

NOTE: ***The House of Delegates will convene at the Sheraton-Palace Hotel; all scientific sessions and exhibits will be at the Civic Auditorium.***

Eighty-fourth Annual Session
CALIFORNIA MEDICAL ASSOCIATION
San Francisco, California
MAY 1-4, 1955

HOTEL ROOM RATES*

	Single	Double	Twin Beds	Suites
SHERATON-PALACE HOTEL Market and New Montgomery	7.50-15.00	10.00-17.50	10.50-18.00	19.00-65.00
ST. FRANCIS HOTEL Powell and Geary	9.00-20.00	11.00-16.00	13.00-22.00	24.00-40.00
SIR FRANCIS DRAKE HOTEL Powell and Sutter	8.50-14.00	10.50-16.50	13.00-19.50	25.00-36.00
CLIFT HOTEL Geary and Taylor	10.00-15.00	10.00-18.00	13.00-18.00	18.00-35.00
PLAZA HOTEL† Post and Stockton †Deposit required	6.00-7.00	.....	9.00-10.00	.....
STEWART HOTEL Geary and Powell	4.50-8.00	6.50-10.00	7.00-12.00	12.00-17.00
WHITCOMB HOTEL Market and Eighth	5.00-9.00	7.00-11.00	8.00-12.00	18.00-25.00
ALEXANDER HAMILTON O'Farrell and Hyde	6.00-11.00	8.00-13.50	8.50-14.00	12.00-30.00

***The above quoted rates are existing rates but are subject to any change which may be made in the future**

CALIFORNIA MEDICAL ASSOCIATION
450 Sutter Street—Room 2000
San Francisco 8, California

Please reserve the following accommodations for the 84th Annual Session of the California Medical Association, in San Francisco, May 1-4, 1955.

Single Room $..... Double Bedded Room $..... Twin Bedded Room $.....

Small Suite $..... Large Suite $..... Other Type of Room $.....

First Choice Hotel..... Second Choice Hotel.....

ARRIVING AT HOTEL (date).....Hour:.....A.M.....P.M. { Hotel reservations will be held until

Leaving (date).....Hour:.....A.M.....P.M. { 6:00 P.M., unless otherwise notified

THE NAME OF EACH HOTEL GUEST MUST BE LISTED. Therefore, please include the names of both persons for each double room or twin bedded room requested. Names and addresses of all persons for whom you are requesting reservations and who will occupy the rooms asked for:

.....

.....

.....

.....

Individual Requesting Reservations—Please print or type Delegate?..... Alternate?.....

Name..... County.....

Address..... City and State.....

WOMAN'S AUXILIARY
TO THE CALIFORNIA MEDICAL ASSOCIATION

On this page during the past several months you have been introduced to ten of the officers and committee chairmen who help to guide and coordinate the activities of our state Auxiliary. In this issue, we would like to present several more of them and tell you a little about their duties and achievements.

* * *

COURIER IS THE BEST IN THE NATION

Our state magazine, *Courier*, has for many years been rated as the best publication of its kind. Issued five times a year, it is an attractive 20-page magazine reflecting the work and accomplishments of the component county units which make up the largest state Auxiliary in the nation. Editor this year is Mrs. Charles Sprague of East Highlands; Mrs. Horace Sharrocks of Sebastopol is Associate Editor, and Mrs. Francis Howard of San Carlos is Circulation Manager. Executive Director of the magazine is Mr. Robert L. Thomas, assistant Executive Secretary of the California Medical Association.

* * *

PUBLIC RELATIONS IS A BROAD FIELD

Public Relations is not a single program or project, but our day-by-day relations with the public. Good public relations is not something that can be brought about at a single stroke by one person or one committee; it is the sum total of everything we say or do, as individuals and as an Auxiliary.

However, a few specific projects are planned each year in all of our counties to create better public relations and to acquaint the public with the activities, aims and accomplishments of the Medical Association and its Auxiliaries.

Coordinating the work on a state level is Mrs. Theodore Poska of Eureka, who stresses the importance of 100 per cent membership participation in creating good public relations. She cooperates with the chairmen of Program, Nurse Recruitment, Mental Health, and Legislation in planning projects and activities that will reflect the Auxiliary's sincere interest in Community Service.

* * *

WE OPERATE ON A BUDGET

Since we are a large organization, with nearly 6,000 members, we handle thousands of dollars annually. Every member pays $1 in dues to the national Auxiliary and $1 to the state Auxiliary, plus the dues set by her own county, which may vary from about $3 to $5 a year. Mrs. Arthur Hurd of San Marino has the responsible job of treasurer; Mrs. Floyd K. Anderson of Los Angeles is finance chairman. Serving with these two officers to form the Finance Committee is the former treasurer, Mrs. Newell Jones of Encino. All bills incurred by the Auxiliary must be approved by this committee and a voucher is made for every expenditure. Our books are audited on April 15 each year, and a complete financial report is made to the membership in May.

* * *

OUR ACHIEVEMENTS ARE RECORDED FOR POSTERITY

And that is the work of our Historian, Mrs. Bryson Cox of Fresno. She compiles a detailed history of the work we accomplish during the current year and places it in our files at the C.M.A. office in San Francisco. She also sends a copy to the National Historian, and she makes a brief oral report at the State Convention in May. She collects significant publicity from the counties for a scrapbook of news clippings, and collects yearbooks, printed programs and any other material of historical or reference value.

* * *

THE REVISIONS COMMITTEE WORKS WITH THE ADVISORY BOARD

The Committee on Revisions considers all proposed amendments to the Constitution and By-Laws of the Auxiliary and presents them to the Convention delegates for their consideration. An affirmative vote of at least two-thirds of the voting members is required, and the amendments must first have been approved in writing by the Advisory Board of the California Medical Association.

Chairman of this very important committee is Mrs. William W. Newman of San Francisco, a past County President and a former State Board member. Also serving on the committee is the State Parliamentarian, Mrs. Carl Burkland of Sacramento, junior Past President of the State Auxiliary.

* * *

PICK A HOTEL

It isn't too soon, is it, for a doctor who plans to attend the C.M.A. Annual Session in May to discuss with his wife where they will stay while they are in San Francisco? [See information regarding housing accommodations, page 140.]

MRS. FREDERICK J. MILLER, *President*

NEWS & NOTES

NATIONAL • STATE • COUNTY

LOS ANGELES

Dr. Ewing L. Turner of Los Angeles was elected president of the Los Angeles County Medical Association for the year 1955 at the annual elections held in December. He succeeds Dr. J. Philip Sampson of Santa Monica. Dr. Orville W. Cole of Long Beach was elected vice-president and Dr. J. Norman O'Neill of Los Angeles was elected secretary-treasurer.

* * *

Jefferson Medical College Alumni of Southern California will sponsor a banquet during the annual scientific assembly of the American Academy of General Practice which is to be held in Los Angeles March 28-31. The banquet is scheduled for Tuesday, March 29, in the Statler Hotel. Cocktails will be served at 7 o'clock and dinner at 8. Information and reservations may be obtained from Dr. J. Elder Bryan, Jr., 6253 Hollywood Boulevard, Los Angeles 28.

* * *

Dr. Peter V. Lee, formerly a member of the faculty of the Stanford University School of Medicine, has been appointed assistant dean of the University of Southern California School of Medicine. Dr. Lee will assist Dean Gordon E. Goodhart with administrative affairs and will also serve as assistant professor of pharmacology and toxicology.

* * *

Officers elected by the **Metropolitan Dermatological Society** of Los Angeles for 1955 are: President, Dr. Irving A. Lewe, Montebello; vice-president, Dr. Harold Price, North Hollywood; and secretary-treasurer, Dr. Edward L. Murphy, Burbank.

* * *

Dr. Myron Prinzmetal, attending physician at Cedars of Lebanon Hospital, has been named among the ten winners of the 1955 **Modern Medicine Award for Distinguished Achievement.** Announcement of the award was made by Dr. Walter C. Alvarez, editor in chief of *Modern Medicine* magazine. Dr. Prinzmetal, who is also associate clinical professor of medicine at the University of California, Los Angeles, received the award for his advancement of understanding of the physiology and treatment of heart disease. He is also a member of the National Advisory Heart Council.

* * *

The Third National **Air Pollution Symposium** is scheduled to be held April 18-20 in Pasadena. The program now planned will cover the areas of new analytical techniques and instrumentation, physiological effects of air pollution on plants and animals, and legal and management aspects of the air pollution problem.

SAN FRANCISCO

The fourth biennial **Western Conference on Anesthesiology** will be held in San Francisco, March 21-23.

* * *

The first **Medical Service Personnel Procurement** office for the Regular Army and Army Reserve has been opened at Stillwell Hall, Presidio of San Francisco.

The office was established to facilitate the release of information about the Army Medical Service to doctors, dentists, veterinarians, Medical Service Corps and Women's Medical Specialist Corps.

Major Frederic C. Buck, who was given the assignment of opening the office, will handle inquiries on the doctor's draft law, Army internship and residency programs, opportunities and benefits in the medical service, graduate professional education programs, and specialist opportunities in the Army.

* * *

The **Western Industrial Medical Association** will hold its fourteenth annual meeting in San Francisco, Saturday, April 30, the day before the opening of the California Medical Association's Annual Session. The meeting, which is to be in the Empire Room of the Sir Francis Drake Hotel, will start at 8:15 in the morning and close at 5 in the evening.

SAN MATEO

Dr. James S. Edwards of San Carlos has been installed as president of the San Mateo County Medical Society. He succeeds Dr. Bradley C. Brownson of San Mateo. Dr. Norman C. Fox of San Carlos, secretary-treasurer last year, was elected president-elect, and Dr. Henry A. Brown of San Mateo was elected secretary-treasurer.

SONOMA

The third annual meeting of the **California Blood Bank System** will be held in Santa Rosa, February 25-27. Besides medical aspects of blood banking and discussions of the therapeutic uses of blood and blood fractions, there will be committee reports, discussion of administrative matters and election of officers. Major General William F. Dean, United States Army, will be guest speaker at a dinner meeting Saturday evening, February 26.

GENERAL

The next available appointment for the **Earl D. Osborne Fellowship in Dermal Pathology** begins July 1, 1955, according to recent announcement by the American Academy of Dermatology and Syphilology which sponsors the fellowship. Purpose of the fellowship is to provide annually the opportunity for study and training in dermal pathology to a postgraduate student who has completed satisfactorily at least one year or preferably two years of training in dermatology. **The stipend** is $4,000 a year, divided into four quarterly payments during the year's fellowship. The period of training will be spent at the Armed Forces Institute of Pathology, Washington, D. C., the appointment being subject to approval by the director of the Institute. The American Board of Dermatology and Syphilology, Inc., has approved the Institute as an institution for one year of training. It is required that a student must complete one year of graduate training, either before or after completion of the Osborne Fellowship, in an institution approved by the Board for three years of training.

Dermatologists in training who are interested in this fellowship may obtain application blanks from Dr. Hamilton Montgomery, chairman of the Committee on Pathology of the American Academy of Dermatology and Syphilology, 200 First Street Southwest, Rochester, Minnesota.

* * *

The International College of Surgeons is offering a scholarship to a young Canadian or American surgeon who wishes to study abroad, the organization announced recently. The scholarship will be in the amount of $3,000 to pay for transportation and living expenses for a period of 12 months. The physician selected will be expected to spend at least ten months of the year as a resident or fellow in a teaching center in one of the countries of Europe or South America. Details concerning the qualifications of applicants may be obtained from The Scholarship Committee, International College of Surgeons, 1516 Lake Shore Drive, Chicago 10, Illinois.

* * *

The first **Medical Service Personnel Procurement** office for the Regular Army and Army Reserve has been opened at Stillwell Hall, Presidio of San Francisco.

The office was established to facilitate the release of information about the Army Medical Service to doctors, dentists, veterinarians, Medical Service Corps and Women's Medical Specialist Corps.

Major Frederic C. Buck, who was given the assignment of opening the office, will handle inquiries on the doctor's draft law, Army internship and residency programs, opportunities and benefits in the medical service, graduate professional education, programs, and specialist opportunities in the Army.

POSTGRADUATE EDUCATION NOTICES

UNIVERSITY OF CALIFORNIA AT LOS ANGELES

Announces the following spring courses:

Application of Principles of Industrial Medicine to Private Practice—February 2-March 23, 1955.

Treatment of Emotional Problems in Office Practice—February 10-April 14, 1955.

Removal of Foreign Bodies from Lung and Bronchi—February 11-12, 1955.

Photomicrography—February 16-March 23, 1955.

Dermatology in General Practice—February 16-March 23, 1955.

Pathological Physiology—February 21-May 9, 1955.

Advanced Psychiatric Case Seminar—March 1-April 19, 1955.

Annual Surgical Lecture Series—March 9-May 25, 1955.

Diagnostic Psychological Testing—April 14-May 9, 1955.

Plastic Repair of Superficial Wounds—April 22 and 23, 1955.

Techniques of Surgery of Malignancies of Oral Cavity, Maxillary, Parotid Gland and Neck—April 25 and 26, 1955.

Physiology, Anatomy and Surgery of the Temporal Bone—April 28, 29, 30, 1955.

Surgical Anatomy of the Thorax, Abdomen and Pelvis—April 28-May 23, 1955.

Obstetrics and Gynecology—early May.

Fevers of Unexplained Origin with Emphasis on Brucellosis—May, 1955.

4th Annual Laboratory Technicians Symposium—June 18 and 19, 1955.

Contact: Thomas H. Sternberg, M.D., Head of Division, Office of the Dean, School of Medicine, Division of Postgraduate Medical Education, U.C.L.A., Los Angeles 24.

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

In San Francisco:

Electrocardiography for Beginners—January 31 to February 4.

Advanced Electrocardiography—January 31 to February 4.

Therapy of Cardiovascular Diseases—January 31 to February 4.

Atomic Energy Medicine—February 24 to February 27.

Course for General Practitioners—March 7 to March 11.

Symposia on Psychosomatic Medicine—March 23, 30, and April 6.

Recent Advances in Internal Medicine—April 18 to April 22.

Pediatric Conference—September (dates to be announced later).

Conference on Applied Therapeutics—October 17 to October 19.

Conference on Gynecology and Obstetrics—October 20 and October 21.

Ophthalmological Conference—December 5 to December 9.

In East Oakland:

Medicine for General Practitioners—Tuesday evenings, September 20 to December 6.

In Berkeley:

Postgraduate Conference—Wednesday evenings, September to December (dates to be announced later).

In San Mateo:

Evening Lectures in Medicine—Thursday evenings, September 22 to December 15.

Contact: Office of Medical Extension, University of California Medical Center, San Francisco 22.

STANFORD UNIVERSITY SCHOOL OF MEDICINE, SAN FRANCISCO

Spring Conference in Ophthalmology—March 21 through March 25.

Contact: Office of the Dean, Stanford University School of Medicine, 2398 Sacramento Street, San Francisco 15.

UNIVERSITY OF SOUTHERN CALIFORNIA AT LOS ANGELES

The Medical Extension Education Division of the University of Southern California School of Medicine announces:

Four Courses to be offered for twelve weeks starting January 6, 1955, as follows:

No. 841 Course — Basic Principles of Cardiorespiratory Physiology and their Clinical Application.*

No. 873 Course—Cardiac Resuscitation—Sponsored by the Los Angeles County Heart Association.

No. 864 Course—Pediatric Clinics for General Practitioners.

No. 846 Course—Seminars in Advanced Gastroenterology.

Contact: For application blanks or other information call or write to Division of Medical Extension Education, University of Southern California School of Medicine, 2025 Zonal Ave., Los Angeles 33, Calif. (CApitol 5-1511).

CHILDREN'S HOSPITAL SEMINARS

The Management of Metabolic Disturbances Commonly Encountered in Practice—January 22, 1955.

The Allergic Dilemma—February 26, 1955.

Infections and Their Management—March 26, 1955

Accreditation by the Board of General Practice has been granted. Gertrude F. Jones, M.D., Chairman, Medical Alumni Committee, Children's Hospital, 3700 California Street, San Francisco 18.

CALIFORNIA MEDICAL ASSOCIATION, POSTGRADUATE ACTIVITIES INSTITUTES

West Coast Counties—Santa Barbara—February 17-18, 1955.

San Joaquin Valley Counties—Yosemite—April 13, 14, 15, 1955.

Sacramento Valley Counties—Cal-Neva—June 16-17, 1955.

Contact: C. A. Broaddus, M.D., Director of Postgraduate Activities, P.O. Box AI, Carmel, California.

*Course No. 841 is restricted to specialists—all other courses are open to graduates of Grade A Medical Schools who have completed an approved internship.

Medical Dates Bulletin

This bulletin of the dates of postgraduate education assemblies and the meetings of various medical organizations in California is supplied by the Committee on Postgraduate Activities of the California Medical Association. In order that they may be listed here, please send communications relating to your future medical or surgical programs to: C. A. Broaddus, M.D., P.O. Box AI, Carmel, California.

FEBRUARY MEETINGS

February 26—Children's Hospital Seminar: The Allergic Dilemma. Gertrude F. Jones, M.D., chairman, Medical Alumni Committee, Children's Hospital, 3700 California Street, San Francisco 18. Accreditation by the Board of General Practice has been granted.

MARCH MEETINGS

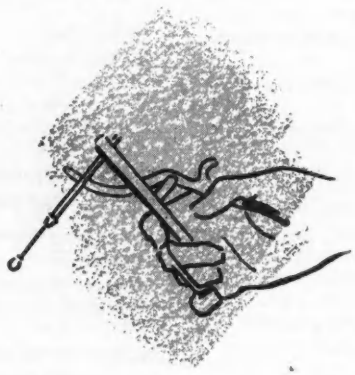
March 26—Children's Hospital Seminar: Infections and Their Management. Gertrude F. Jones, M.D., chairman, Medical Alumni Committee, Children's Hospital, 3700 California Street, San Francisco 18. Accreditation by the Board of General Practice has been granted.

* * *

California Medical Association: Annual Session, May 1-4, 1955, San Francisco.

American Medical Association: Annual Session, 1955, Atlantic City, June 6-10; Clinical Session, 1955, Boston, November 29-December 2.

California Society of Internal Medicine: October 1, 1955, Biltmore Hotel, Santa Barbara, Mildred D. Coleman, Secretary, 384 Post Street, San Francisco 8.



INFORMATION

Health Insurance and Medical Practice in Germany

GEORGE M. FIRESTONE, *M.D.*, Santa Rosa

ALTHOUGH MUCH has appeared in the American literature on the practice of medicine in Great Britain since the enactment of its national health laws, very little has been presented on similar problems in other countries. The author had the opportunity during 1953, while on a tour of duty with the United States Army, of observing the practice of medicine in Germany.

At first glance, medical practice in Germany seems to exist much as it does in the United States, since almost 60 per cent of German physicians are in private practice. But when one notes that 80 to 90 per cent of the population have prepaid health insurance, the conclusion is apparent that a physician in "private practice" cannot exist unless he is at the same time on the panel of one or more of the health insurance companies.

Although much of the health insurance in Germany is written by private companies, the operations of these companies are governed strictly by federal law. The historical development of this situation is of interest.

The basic philosophy of government and responsibility in Germany has always been distinctly different from that in the United States. In the United States the individual citizen has always been the prime mover and has established a government characterized by specific limitations of its powers so that it will always be subordinate to him. On the contrary, in Germany, governments beginning in the Middle Ages have been centralized in the hands of the chiefs of government, be they feudal lord or prince. The individual living under his jurisdiction has had little to say regarding the decisions of this government until very recent years, namely the end of the Nineteenth Century. Indeed, during much of the period before this, the individual "citizen" was at worst a slave and at best a "share cropper" with all the dependency that this implies. Later, even with the development of "democracy" the people of the country retained the habit of looking not to themselves but to the government for all leadership and help in economic, social and political matters.

With the advent of the industrial revolution and the movement of people from rural areas into the cities, a large working class developed which had lost the few social and economic safeguards it had previously possessed and was left stranded with a low income and marginal subsistence. A similar thing happened in the United States, but, because of a different basic philosophy, the individual here sought to improve his own status with little help or interference from the government. In Germany the government assumed the responsibility for coping with this situation. Accordingly, between 1845 and 1911 a series of laws establishing numerous social benefits were enacted under the German Kaiser. These included the establishment of compulsory prepaid health insurance for certain classes of workers as well as accident insurance, compensation laws, old age insurance, and "invalidism" insurance. As a result of these laws all classes of people other than those who were self-employed or those who were on a monthly salary were brought under a compulsory health program. Since that time, health insurance companies have also been developed for salaried individuals, and other companies have come into existence to take care of the self-employed. At present 80 to 90 per cent of the population of Western Germany is covered by prepaid health insurance. Insurance against sickness is compulsory for those whose income is less than 6,000 DM* a year. Unemployment, old age and invalidism insurance is compulsory for all whose yearly income is less than 9,000 DM. Half the insurance premium is paid by the employee, half by the employer.

These insurance plans, although governed by federal German law, are operated individually by private companies or local government districts. Large factories, local rural districts, individual cities, and federal government "corporations" such as the German railway, operate their own companies, each a company for the benefit of the wage earners under its jurisdiction as well as for all members of the workers' families. A second group of private companies (Ersatzkassen) supplies prepaid insurance to salaried individuals of the "white collar class." There is a third group of private health insurance companies, like companies in the United States, that reimburse the patient for a portion of his medical expenses according to the premiums he pays, but do not provide a prepayment plan. Other insurance companies have been formed to pay for dental expenses, orthopedic appliances and glasses.

Submitted August 31, 1954.

*One DM (DeutschMark) equals approximately $0.27 American.

The prepaid health insurance plans as operated by the first two groups of insurance companies, finance almost all medical care that a patient may require. This includes payment of the patient's physician for his services, for diagnostic workup and treatment, payment of the complete hospital bills, payment for all drugs purchased from pharmacies (except for a 0.50 DM prescription fee which the patient pays). It also includes transportation for the patient from his home to the physician's office or hospital, including street cars, buses or trains, and in addition to the above, includes a .50 DM fee per day to all hospitalized patients for "pocket money." Patients who are confined to bed at home are paid a variable proportion of their basic income for the duration of their illness. The insurance does not cover preventive medicine, nonessential plastic surgical treatment, difficulties due to old age, hereditary disease, pneumothorax, employment examinations or normal pregnancies and deliveries.

In 1950 there were 63,000 physicians in West Germany, according to official estimate. Of these approximately 36,500 were self-employed, while 27,000 worked on salary for a hospital or other organization. In 1953 (when the author was in Germany) these figures had not changed much. The total population of West Germany in 1953 was 48,000,000, making an overall ratio of one physician to 750 persons. According to most local sources this represented an oversupply of physicians and was largely due to three factors. The first was the policy of the German government during World War II to increase the number of students in medical schools. The second was the currency reform program of 1948, which wiped out almost all private savings in Germany and so prevented older physicians from retiring as they might otherwise have done. The third factor was the postwar migration from Germany's east zone of large numbers of physicians who, like others of the middle class, found that they could not exist under the Communist regime.

The average self-employed physician in Germany nets approximately 700 DM a month. In terms of buying power this would compare to approximately $400 a month in the United States. In order to receive this income, a physician must see approximately 50 patients a day. Physicians employed by hospitals receive monthly pay according to the following schedule: Interns, between 50 and 120 DM; ward physicians, 500 to 700 DM; assistant chiefs of service, 600 to 800 DM; chiefs of service, 800 to 1,000 DM.

Since between 80 and 90 per cent of the population is covered by prepaid health insurance, a self-employed physician finds it practically impossible to exist unless he has a contract from a health insurance company. At present it is almost impossible for a new physician to be placed on an insurance company panel unless he can find work as assistant to a man already on the panel, or has a special "pull" with the company. Similarly it was difficult prior to 1953 for a young physician to find employment in a hospital although this situation has now eased somewhat. The net effect of the control of medical practice panels by the insurance companies has been that many physicians have been forced to seek employment outside their profession, and all in private practice must follow the wishes of the companies or risk losing their contracts.

Physicians and hospitals in Germany do not receive payment for their services directly from the health insurance companies. The health insurance companies function to collect premiums, paid partly by employer and partly by employee, which are proportionate to the wages of the insured workers. The funds so collected are paid to a clearing house, which, in turn, has received claims for services from all the physicians on the panels of the particular company concerned. The insurance companies pay a fixed fee to the clearing house per patient per quarter year. The clearing house must then divide this money among the claimant physicians according to the types and number of procedures performed by each physician in the preceding period.

Since the insurance companies are local organizations operating in small areas, it is immediately obvious that if a company is operating in a field where its members receive low wages or where there is much unemployment, the physicians will receive little for their services. On the other hand, physicians on the panel of a company operating among a well paid group will receive higher remuneration for the same services. Unemployment is a particularly important factor since the health insurance company is required by German law to continue to pay for medical services for its members whether they are employed or unemployed. However, an unemployed person is required to pay no premium to the insurance company.

In addition to all this, the physician is limited in the number of claims he can submit for payment, since the insurance companies have ruled that a physician will be compensated for only a certain number of any one procedure per month. For example, a physician can claim payment for only so many house calls per month. He will not receive payment for any calls he makes above this arbitrary number.

In the case of hospital patients, the insurance company pays a fixed fee to the hospital per patient-day regardless of the type of case or the amount of care required. As in the case of payments to physicians, the specific fee depends on the available

funds of the insurance company. As this fee must cover laboratory, operating room and physicians' salaries, as well as almost all the other expenses of running a hospital, the expenditures for each of these services must be scrutinized by the hospital director so that he may keep within his budget. In addition the insurance companies employ physicians whose sole function is to check on treatments both in and out of hospitals so that expensive drugs or procedures will not be used where something else "will do."

The health insurance companies have contracted to pay for all drugs prescribed except for a small fee of 0.50 DM which is assumed by the patient on each prescription. However, the insurance companies have set a policy of paying no more than a prescribed fee to the druggist per patient per quarter year regardless of specific drugs used. In the area in Germany in which the author resided, this amounted to 4.50 DM per patient per quarter year. It is true that drugs in Germany are somewhat less expensive than in the United States. Also the physician may prescribe expensive drugs for some patients if he prescribes correspondingly less for others. The only concern of the insurance companies is that the total drug cost for all the patients on the physician's panel will be within the allowed figure. It is obvious, however, that with this type of system the physician must be concerned more with the economics of drug therapy than with the indications in any given case.

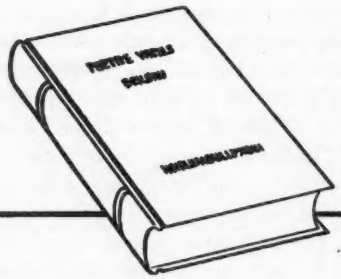
Self-employed physicians have control of their patients only as these patients are seen in their offices or at home. When a patient is hospitalized, care of him is turned over to the staff of the hospital, the local physician having no further contact with the patient until he has been discharged from the hospital.

In this brief discussion, the author has made no effort to describe the quality of patient-care or the current level of medical knowledge in West Germany, since that is another problem. An insight into the former might be gained, however, from the observations that "insurance" patients in hospitals are usually given what is called "third class accommodations"; from the further observation that the average physicians must see about 50 patients per day in order to earn his "average" income; and from the fact that the cost of treatment is controlled by the insurance companies.

In summary it may be noted that the German tradition of looking to government for all social and economic aid has led to a system of federally supervised compulsory prepayment health insurance covering almost 90 per cent of the population of West Germany. It has become the rule for the insurance companies to dictate the cost and therefore the amount and quality of inpatient and outpatient services which the patient receives. It has been possible for the insurance companies to hold an economic club over the physician and thus control both him and his practice.

(Perhaps the best illustration of this situation is the deliberate omission from the authorship of this article of the name of the German physician who collaborated in assembling the material presented here, and without whose help this paper would not have been possible. This omission was made at his direct request despite his agreement with the facts and conclusions presented, since by the mere fact of his association with the authorship of an article of this type he would subject himself to the possible reprisals of the insurance companies on which his livelihood depends.)

1180 Montgomery Drive, Santa Rosa.



THE PHYSICIAN'S *Bookshelf*

ISOTOPIC TRACERS—A Theoretical and Practical Manual for Biological Students and Research Workers. G. E. Francis, Reader in Biochemistry, St. Bartholomew's Hospital Medical College; W. Mulligan, Senior Lecturer in Biochemistry, Glasgow University Veterinary School, and A. Wormall, Professor of Biochemistry, St. Bartholomew's Hospital Medical College. University of London, the Athlone Press, 1954. Distributed by John de Graff, Inc., 64 West 23rd Street, New York 10, 1954. 306 pages, $7.00.

This book is divided into two parts. In the first part the theoretical principles underlying the preparation and measurement of radioactive and stable isotopes, their use as biological tracers, practical information concerning techniques, instrumentation, hazards and precautions in the use of radioactive isotopes, etc., are discussed.

The second part of the book contains detailed instructions for a course of practical exercises.

This book represents a summation of the lectures and demonstrations given by the authors at the St. Bartholomew's Hospital Medical College. These lectures particularly were adapted to meet the needs of selected undergraduates and graduates in science or medicine taking the London Hons. B. Sc. (Special Physiology) examination. These candidates had used or desired to use isotopes in their own researches in biochemical and physiological investigations.

The equipment described and used in this book was manufactured in Great Britain.

The authors emphasize that there is a real and increasing need for training centers where biological workers can acquire a knowledge of, and particularly practical instruction in, the use of Isotopic Tracer Methodology.

It is the hope of the authors that this book will be used as a practical laboratory handbook rather than a library reference book.

This book will be a valuable addition to the armamentarium of all biological students and research workers. The use of radioactive isotopes for diagnostic and therapeutic purposes has attained a prominent position in both the clinical and research aspects of medicine. This book will be of limited interest to the physician not directly concerned with the use of isotopes for investigation.

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PRACTICE OF ALLERGY. Warren T. Vaughan, M.D., Richmond, Va. Third Edition revised by J. Harvey Black, M.D., Dallas, Texas. The C. V. Mosby Company, St. Louis, 1954. 1164 pages, $21.00.

This *Practice of Allergy* by Warren T. Vaughan, with additions and revisions by one of his many friends, J. Harvey Black, also a renowned pioneer in allergy, continues to be the most important extended treatise in the field of clinical allergy. The profession is fortunate that this masterfully conceived and written volume continues to be available for present day students and also physicians in other specialties who are interested in clinical allergy, all of whom should know this contribution and have it readily available for frequent reference. Dr. Black's many additions and revisions, moreover, justify the possession of either the second edition or especially this third edition even though the first edition has been in the physician's library for many years.

Dr. Vaughan's authoritative discussion of the history, terminology, experimental anaphylaxis and its identity to clinical allergy, and the immunology and pathology of clinical allergy have required little or no revision. His chapters on the frequency of allergy, heredity, minor and major allergies, the effects of climate and environment, the methods of history taking, skin testing, passive transfer, mucous membrane and patch tests, and other diagnostic procedures have changed little since the first edition. The specialty owes a great debt to Dr. Vaughan for his discussion and emphasis of clinical food allergy, along with the equally important inhalant allergy. The study of food allergy through history and diet trial and the errors inherent in test-negative diets receive proper attention in this work. The origin and relationship of all foods and condiments are important for reference. The section on pollens, the revised surveys of all individual states and other countries, and the diagnosis and treatment of pollen allergy are duly stressed and amplified. The book retains a most informative discussion and classification of fungi and discussion of the diagnosis of fungus allergy and the relative importance of fungi in clinical problems. Bacterial allergy continues to be, in the writers' opinions, of minor clinical importance. Drug allergy, of increasing frequency before and since the first edition of the book, receives present day consideration. The use and indications for cortisone and corticotropic hormone and the antihistamines are discussed. The causes of contact allergy and the accepted methods of study are presented.

New and important chapters on pulmonary function studies, the physiologic interpretation of clinical allergy, including the work of Selye, perennial hay fever, important additions to the pharmacology of allergy, histamine cephalalgia, the most recently revised elimination diets with their menus and recipes, and other subjects and phases of clinical allergy have been included by Dr. Black. In future additions a main challenge will be a more extended discussion of the many manifestations of allergy as encountered in practice.

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MANAGEMENT OF PAIN, THE—With Special Emphasis on the Use of Analgesic Block in Diagnosis, Prognosis, and Therapy. John J. Bonica, M.D., Director, Department of Anesthesia, Tacoma General and Pierce County Hospitals; Clinical Associate, Department of Anatomy, University of Washington Medical School. Lea & Febiger, Philadelphia, 1953. 1533 pages, 785 illustrations on 44 figures and 52 tables, $20.00.

Since pain is the most common organic symptom which compels the patient to seek medical assistance, it is to be expected that a monograph on its management could justi-

fiably include a major segment of the problems of clinical practice. As Bonica's discussion is followed, it develops that this book lives up to such an expectation. Entities from the neuralgias and control of pain in terminal cancer to such unexpected and tenuously related subjects as diabetes mellitus and megalocolon are considered. The discussion includes not only the technical aspects of pain management, but etiology, pathologic physiology, symptomatology, and differential diagnosis of many situations. The evaluation of therapy deals with both medical and surgical methods, as well as the interruption of pain pathways. Though theory is not the principal thesis of the book, the anatomic and physiologic factors of pain as we think of them today have not been omitted.

There are some controversial proposals which seem to be handled dogmatically, but such is the author's prerogative; in general, the discussion is sound and well supported. The substantial bibliography will serve as a basis for more extensive delving into the field by any who may be so minded.

An encyclopedia of therapeutic possibility rather than an attempt at a major contribution to fundamental understanding of pain, the volume will have something of value for most clinicians.

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APHASIA THERAPEUTICS. Mary Coates Longerich, Ph.D., and Jean Bordeaux, Ph.D. The Macmillan Company, New York, 1954. 185 pages, $3.75.

This is a short book which should be of considerable value to workers in the field of retraining patients with aphasia. It can be read with profit both by the individual directly responsible for the training, and by the physician who directs the training. The treatment is strictly practical, and it is in this regard that the book has its greatest use.

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DIENCEPHALON — Autonomic and Extrapyramidal Functions. Walter Rudolf Hess, M.D., Professor of Physiology, Emeritus, University of Zurich, Switzerland. Grune and Stratton, New York, 1954. 79 pages $4.00.

This is a brief account of Professor Hess's exploration of the function of the diencephalon by means of his highly developed technique of stimulation and destruction of this portion of the brain in animals. With the greater interest shown in recent years in this region, it is fortunate that this work has been made readily accessible to English speaking neurophysiologists.

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CLINICAL MANAGEMENT OF BEHAVIOR DISORDERS IN CHILDREN. Harry Bakwin, M.D., Professor of Clinical Pediatrics, and Ruth Morris Bakwin, M.D., Associate Professor of Clinical Pediatrics, both of New York University. W. B. Saunders Company, Philadelphia, 1953. 495 pages, 14 figures, $10.00.

The Bakwins have written an encyclopedic book on emotional disturbances in children. They have included a varied and valuable bibliography at the end of each chapter. The book is nicely organized so that normal growth and development and care lead into discussions of emotional disorders of increasing severity. The chapter on history taking and examination of the emotionally disturbed child is for the most part an excellent one as are their chapters on growth and development and psychological testing. The book leans toward present day dynamic concepts of child psychiatry but these concepts are only partly integrated in the material presented. The authors' efforts to include and encapsulate every possible emotional disturbance of childhood both oversimplify much of the material and fail to present some of the evidence which would make certain assertions reasonable. Perhaps the key to the whole book is found in the second word of the title, "management." The effort to instruct the pediatrician on how to "manage" the disorder or the child in a definite, prescribed manner is the book's chief drawback. The prescriptions that follow some excellent descriptions of the disorders illustrate the split between dynamic concepts and dogma. Such statements as "Jealousy begins at two years," "Most infants can be (bowel) trained by 11 to 14 months and some earlier," "Bladder training is best started at 12 to 16 months of age," etc., are illustrative of the arbitrary prescriptions not consonant with present day thinking in child psychology.

One would hope that a textbook which covers such a wide range of children's problems so exhaustively would approach these problems in the light of recent thinking about the child as an integral part of his family and that his emotional illnesses and their treatment would be considered in the same context. This defect is especially evident in their discussions of sleep disturbances, anorexia and obesity.

Perhaps the greatest failing in the book is the attitude that one need only to look to the appropriate chapter and page to find the "open Sesame" to the management of each disorder.

This book's chief value to the pediatrician may be that he will be encouraged to try to handle some of the emotional problems of children himself. When he finds the prescriptions not too helpful he may rely on his own experiences gained in human relationships and may find he can be of some help to the child and his parents.

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PROGRESS IN NEUROLOGY AND PSYCHIATRY—An Annual Review—Vol. IX. Edited by E. A. Spiegel, M.D., Professor and Head of the Department of Experimental Neurology, Temple University School of Medicine. Grune & Stratton, New York, 1954. 632 pages, $10.00.

This perennially excellent review of progress in neurology and psychiatry retains its high standards. The contributors are well chosen, and there is little of the duplication that frequently mars such a composite effort. The reviews are sufficiently detailed to satisfy the specialist; for this reason this is not a book to sit down with of an evening in the hope of being briefly and painlessly brought up to date in the broad aspects of advances in the neuropsychiatric field. It is of much greater value as a short cut to the current literature by those closely associated with the specialties. It is an excellent reference work.

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PSYCHOANALYSIS AND THE EDUCATION OF THE CHILD. Gerald H. J. Pearson, M.D., Dean, Institute of the Philadelphia Association for Psychoanalysis. W. W. Norton & Company, Inc., 1954. 357 pages, $5.00.

Dr. Pearson has written a book of value to everyone concerned with the learning process. Here for the first time, to my knowledge, is assembled much of the psychoanalytic thought on education both historical and current. As is usual with Dr. Pearson, this book is well written in his lucid, easy-to-read style.

From the introduction and from the table of contents one is led to hope for a presentation of the recent developments in understanding of ego psychology as it applies to education. Although part two of the book is labeled "Ego Psychology and the Education of the Child" this is in no way a distillation of current thinking and synthesis of what has been learned from more extensive and intensive therapeutic efforts with psychotic children and adults. The accent is still on oedipal problems, castration fears, repression of sexual curiosity, rather than on the increasing body of information about how the early infant-mother relationship and the

problems of orality affect the capacity to learn. Pearson does mention these in passing, but it is striking how little attention is paid to these fundamental aspects of the child's early experiences and what we have learned is the effect of these experiences on learning and creativity. In this sense the book is disappointing. It is also of interest that the focus of the book is on the individual child and his problems rather than the family and its problems since most educators and persons concerned with mental hygiene in recent years have begun to shift their attention to the total situation from which the learning problems stem. There are also some prescriptions of helpful attitudes for teachers which contain the usual pitfalls of any prescriptions about how someone should behave for someone else's benefit.

Despite these shortcomings, this is a valuable book which should be read by those interested in education and the psychology of learning.

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THE YEAR BOOK OF OBSTETRICS AND GYNECOLOGY—1954-1955 Series. Edited by J. P. Greenhill, B.S., M.D., F.A.C.S., Professor of Gynecology, Cook County Graduate School of Medicine. The Year Book Publishers, Inc., 200 East Illinois Street, Chicago, 1954. 544 pages, $6.00.

The 1954-1955 Year Book of Obstetrics and Gynecology represents the annual review of the literature in this field. It contains in addition the opinions of the editor and his reactions to the various articles. The work is almost evenly divided between obstetrical and gynecological subjects with 247 pages devoted to the former and 229 to the latter. There are 18 titles on toxemia of pregnancy reviewed, 24 on obstetric hemorrhage, and 41 on gynecologic cancer. This is a fairly accurate representation of current interest in these fields. Only 14 titles are devoted to pelvic and obstetric infections. There are 40 pages devoted to operative gynecology.

In general, this issue continues to fulfill the useful and well accepted place which The Year Book has established for itself in obstetrical and gynecological reference works.

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BIOCHEMISTRY AND HUMAN METABOLISM—Second Edition. Burnham S. Walker, M.D., Ph.D., Professor of Biochemistry; William C. Boyd, Ph.D., Professor of Immunochemistry, and Isaac Asimov, Ph.D., Assistant Professor of Biochemistry, all from Boston University School of Medicine. The Williams and Wilkins Company, Baltimore, 1954. 904 pages, $10.00.

The statements of the reviewer concerning the first edition of this textbook (Calif. Med., 77:36, 1952) apply as well to the second edition and some of them will bear repeating. "The book has a freshness and vitality in its outlook and presentation which is distinctive among biochemistry textbooks written for medical students." "The first chapter is devoted to proteins, the basic material in cell structure and function. The authors do not attempt to precisely definite proteins, but describe them as 'large molecules, of molecular weight of the order of several thousand to several million, occurring in the tissues of plants and animals and containing carbon, hydrogen, oxygen and nitrogen, and sometimes other elements, and constructed largely from amino acids.' This definition differentiates proteins from other compounds of biological interest, although not by any means describing this class of substances, whose members differ so much from each other."

The general plan of the book has not been altered in the second edition. In the 78 additional pages the authors have been able to bring the subject matter up to date by reorganizing and partly rewriting Chapter 1 and including Appendix IV on acids and bases of the first edition in this chapter, entirely rewriting Chapter 14 and rewriting parts of most of the remaining chapters.

Although the development of the subject is in the traditional manner, starting with the chemical units of the cells and tissues, namely proteins, amino acids, carbohydrates, fats, nucleic acid structure, etc., the titles for the five major divisions are different, namely I, Structure, containing chapters on Proteins and Amino Acids, Protein Structure, Tissue Chemistry and Blood; II, Control, describing Enzymes and Hormones; III, Growth, on Biochemistry of Nucleoproteins, Cancer and Reproduction; IV, Metabolism, on Food and Diet, Digestion, Diabetes, Lipid Metabolism, Starvation, Electrolytes, etc.; and V, Pathology, limited to Vitamins and Vitamin Deficiency Disease and Infection. There are also three chapters in the appendix on physical chemistry.

The new material includes a table on amino acid composition of proteins, the formula of gramicidin S, a new formula for glucose as *glucopyranose*, kinetics of enzyme action, role of triiodothyronine, adrenocortical hormones, nucleoproteins of viruses, schemes of decarboxylation of amino acids, effects of potassium excess, adoption of conventional skeleton formulas for ring compounds, formula for coenzyme A and role of isotopes in metabolic studies.

One is disappointed in the scant space devoted to metabolic changes in hormone structure and the basic actions of insulin, the omission of important monographs from bibliographies, such as Deuel's extensive monograph on lipids, and the lack of information on chemical effects of heavy metals and other poisons.

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HANDBOOK FOR DIABETIC CHILDREN. Alfred E. Fischer, M.D., Associate Attending Pediatrician, Mount Sinai Hospital, New York City, and Dorothea L. Horstmann, Instructor in Dietetics, Mount Sinai Hospital, New York City. Intercontinental Medical Book Corp., 381 Fourth Avenue, New York 16, N. Y., 1954. 63 pages, $1.75.

This little volume recognizes a definite need, namely information on diabetes which is suited by content and presentation to the young diabetic. Most such booklets refer chiefly to the elderly person whose diet requirements are different and who is likely to need orientation on the arteriosclerotic complications of diabetes.

Its usefulness to the individual doctor in practice will depend on whether his dietetic teaching is in the same philosophy and terminology and whether he can take the time to explore with the child and his parents the facts and feelings necessary to understand and accept his problem. It is a commendable effort to fill a real need but will not take the place of personal interpretation and direction by the doctor.

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SURGICAL UROLOGY—A Handbook of Operative Surgery. R. H. Flocks, M.D., Professor and Head, Department of Urology, and David Culp, M.D., Assistant Professor of Urology, both from the State University of Iowa College of Medicine. The Year Book Publishers, Inc., 200 East Illinois St., Chicago, 1954. 392 pages, $9.75.

"Surgical Urology" is a simply and clearly written book, up to the minute and thoroughly describing most of our present-day urologic operations. In one small volume the authors have ably correlated the physiologic, anatomic and surgical principles involved in operative urology. Numerous clear-cut black and white illustrations add greatly to the value of the book. These illustrations are full page, properly located and, while simply drawn, they permit a good understanding of the text. This is the most informative book of its type that has been published in years, and while quite elementary it would be a valuable addition to the reading table of the beginner or as a reference work for the occasional operator.